MICROALBUMINURIA IN SYSTEMIC HYPERTENSION AND ITS RELATIONSHIP TO TARGET ORGAN DAMAGE

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CERTIFICATE

Certified that this is the bonafide dissertation done by

DR. PRADEEP SREEKUMAR *and submitted in partial fulfillment of the requirements for the Degree of M.D., General Medicine, Branch I of The Tamilnadu Dr. M.G.R. Medical University, Chennai.*

Date : 9/12/2009

Professor Dr. K. UMAKANTHAN M.D
Guide,Professor &
Head of the Department of Medicine,
Coimbatore Medical College,
Coimbatore.

Date :9/12/2009

Dr.V. Kumaran M.S,MCh
The Dean,
Coimbatore Medical College
Coimbatore .

DECLARATION

I solemnly declare that the dissertation titled

"MICROALBUMINURIA IN SYSTEMIC HYPERTENSION AND ITS RELATIONSHIP TO TARGET ORGAN DAMAGE "

was done by me from January 2008 to August 2009 under the guidance and supervision of **Professor Dr. K. UMAKANTHAN**

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Dr.PRADEEP SREEKUMAR

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CONTENTS

INTRODUCTION

Hypertension is one of the most common worldwide diseases afflicting humans. Because of the associated morbidity and mortality and the cost to society, hypertension is an important public health challenge. Over the past several decades, extensive research, widespread patient education, and a concerted effort on the part of health care professionals have led to decreased mortality and morbidity rates from the multiple organ damage arising from years of untreated hypertension. Hypertension is the most important modifiable risk factor for coronary heart disease (the leading cause of death in North America), stroke (the third leading cause), congestive heart failure, end-stage renal disease, and peripheral vascular disease. In this context, assessment of subclinical organ damage has become a key element in evaluating hypertensive patients.

Recognition of microalbuminuria stemmed from diabetes research 4 decades ago. According to National Kidney Foundation microalbuminuria is defined as a Urine Albumin Excretion Rate (UAER) of approximately 30-300mg/d in non ketotic sterile urine. The association between microalbuminuria and hypertension was described long time ago. In 1976, Parving et al highlighted the relation between microalbuminuria and the severity of hypertension. A renewed interest in microalbuminuria and essential hypertension occurred in late 1980s when several studies pointed out the importance of microalbuminuria as an important risk factor

for renal & cardiovascular disease in patients with diabetes and hypertension. Microalbuminuria possibly reflects a state of increased renal endothelial permeability and is an easily measured marker of rather diffuse endothelial dysfunction, low grade inflammation and vascular disease burden. Therefore screening for microalbuminuria and follow up of patients is now a general practice in some countries, but not all.

Microalbuminuria can be diagnosed on the basis of three positive tests – Albumin creatinine ratio; urine albumin excretion rate or a combination of both. Although the determination is yet to be fully standardized, current assessment methods are sufficiently robust to warrant periodic assessment for all hypertension patients.

Great importance has been given to microalbuminuria as a prognostic marker of cardiovascular and/or renal risk in hypertensives.Studies have demonstrated an ongoing association of microalbuminuria with cardiovascular events and kidney lesions, that is, the higher the urinary albumin excretion the greater the risk to develop these conditions .

AIMS AND OBJECTIVES

1. To detect prevalence of microalbuminuria in systemic hypertension.

2. To document the involvement of various organ systems in these patients and study relationship of microalbuminuria to target organ damage.

REVIEW OF LITERATURE

The phenomenon of hypertension was 1st characterized at the turn of the century when Riva Rocci developed the prototype of modern sphygmomanometer and so allowed routine measurement of BP. Korotkov then perfected the sphygmomanometric technique by describing the sounds heard over brachial artery as the pressure in the cuff is reduced[1].

Defining Hypertension:

Blood pressure is a continuous variable with no absolute dividing line between normal and abnormal values. The best operational definition is "the level at which the benefits (minus the risks & costs) of action exceeds the risks and costs (minus benefits) of inaction. In past several decades, the levels at which definite HT is defined as beginning have changed from > 160/95mms of Hg to > 140/90 mms of Hg. The definition of HT for home & ambulatory measurements are different: BP > 135/85 mms of Hg for 24hours ambulatory monitoring or home monitoring is the usual level considered to be where HT starts[2].

Classification of BP: (For adults aged 18 yrs or older)

JNC – VII Classification: (American Medical Association.) [34]

BP Classification	Systolic BP(mm Hg)	Diastolic BP(mm Hg)
Normal	<120	<80
Pre hypertension	120 – 139	80 – 89
Stage I HT	140 – 159	90 – 99
Stage II HT	≥ 160	≥ 100

ESH – ESC Guidelines: 2003: for management of HT. [European Society of HT – European Society of Cardiology].

Category	Systolic BP(mm Hg)	Diastolic BP (mm Hg)
Optimal	<120	<80
Normal	<130	<85
High Normal	130 – 139	85 – 89
Hypertension	140- 159	90 – 99
Stage 1		
Stage2	160 – 179	100 – 109

Stage 3	$\geq$ 180	110
Isolated systolic HT	$\geq$ 140	90

The JNC VII classification is based on the mean of 2 or more properly measured seated BP readings on each of 2 or more office visits[3].

Natural history of untreated Hypertension:

In untreated Hypertensives, with age, the systolic BP increases and diastolic BP falls. The risks associated with HT are much more strongly related to levels of systolic BP, than to Diastolic BP in those over the age of 50 – 60 years.

Symptoms and Signs:

Uncomplicated HT is almost always asymptomatic so that patients may be unaware of the consequent progressive cardiovascular damage for as long as 10 – 20years. Symptoms often attributed to HT $\rightarrow$ Headache, Tinnitus, Palpitation, Dizziness and fainting – may be observed just as commonly in normotensive population.

Headache is characteristic of only severe HT: Such headaches are localized to occipital region and are present when the patient awakens in the morning but subsides spontaneously after several hours.

Complaints referable to vascular disease are the following :

Epistaxis, hematuria, blurring of vision owing to retinal changes, episodes of weakness/ dizziness due to transient cerebral ischemia, angina pectoris, dyspnoea due to cardiac failure. Pain due to dissection of aorta / leaking aneurysm is a rare presenting symptoms[2].

Course of untreated HT:

The relation between increasing BP and cardiovascular mortality is direct, continuous and independent of other risk factors. The findings in long follow up of subjects screened for MRFIT study have been confirmed by meta analysis of relationship between BP and cardiovascular mortality in almost one million adults in 61 prosepective observational studies. Each 20 mm Hg rise in systolic BP or 10 mm Hg rise in diastolic BP is associated with > a 2 fold increase in mortality from stroke and a 2 fold increase in mortality from CAD.

Risk Stratification In Patients With Hypertension :

Major Risk factors	**Target organ Damage**
Smoking	Heart diseases, LVH
Dyslipidemia	Angina / Prior MI

Diabetes mellitus	Prior coronary revascularisation
Age > 60 years	Heart failure
Sex (male and post menopausal female)	Stroke or TIA
Family history of Cardiovascular disease	Nephropathy
Women >65 years and men > 55 years Peripheral arterial disease	Retinopathy

Risk Stratification And Treatment :

Bloodpressure stages	Risk Group A	Risk Group B	Risk Group C
(mm Hg)	No risk factors No TOD* No CCD**	At least 1 risk factor Not including DM NoTOD / CCD	TOD/ CCD and or DM with or without other risk factor
High normal (130 – 139 / 85 – 89)	Life style modification	Life style modification	Drug therapy
Stage I (140 – 159/ 90 – 99)	Life style modification upto (12 months)	Life style modification (upto 6 months)	Drug therapy
Stage II (>160/ >100)	Drug therapy	Drug therapy	Drug therapy

* Target organ damage

** Clinical cardiovascular disease

Complications of Hypertension :

The biological aggressiveness of given level of HT varies among individuals. The pathological hall marks of uncontrolled HT is accelerated atherosclerosis. If untreated, about 50% of hypertensive patients die of Coronary Artery disease (CAD) or Congestive Cardiac Failure (CCF). 33% die of stroke; 10 – 15% die of Renal Failure. The role of HT in producing underlying vascular damage that leads to these cardiovascular catastrophes is usually underestimated. Death is usually attributed to stroke or myocardial infarction instead of to the HT that was largely responsible. The inherent propensity to induce vascular damage can best be ascertained by examination of eyes, heart and kidney.

FUNDOSCOPIC EXAMINATION

Vascular damage in the fundus reflect both hypertensive retinopathy and atherosclerotic retinopathy.Fundoscopic findings provide one of the best indication of the duration of HT and of prognosis. A useful guide is the Keith – Wagener – Barker classification of the fundoscopic changes[1].

Grade I – Localised spasm or narrowing of arteriolar lumen, Arterial tortousity (“ Silver Wiring”).

Grade II – Arteriovenous nicking due to sclerosis of the adventitia and /or thickening of the arteriolar wall.

Grade III – Haemorrhage and exudates due to rupture of small vessels.

Grade IV – Papilloedema

Grade III and IV changes are clearly indicative of an accelerated malignant form of HT.

Cardiac Involvement:

HT places increased tension on the left ventricular myocardium that is manifested as left ventricular hypertrophy (LVH) which accelerates the development of atherosclerosis within the coronary vessels. The combination of increased demand and lessened supply increases the likelihood of myocardial ischemia and there by leads to a higher incidence of myocardial infarction, arrhythmias and congestive heart failure (CCF) in hypertensive patients[2].

Abnormalities in Left Ventricular Function:

Even before LVH develops, changes in both systolic and diastolic function can be seen. Those patients with minimally increased left ventricular muscle mass

may have super normal contractility with a high percentage of fractional shortening and increased wall stress. The earliest functional cardiac changes in hypertension are in left ventricular diastolic function with lower E/A ratios and longer isovolumetric relaxation time. With increasing hemodynamic load, either systolic or diastolic dysfunctions may evolve and progress to different forms of congestive heart failure. In addition, impaired coronary flow reserve and thallium perfusion may be observed in hypertensive patients without obstructive coronary disease.

Left ventricular hypertrophy (LVH) :

LVH results from chronic elevations in arterial pressure that causes cardiac myocyte hypertrophy and remodelling of the coronary resistance vessels. This leads to perivascular fibrosis of the intramyocardial arteries and arterioles. LVH is necessary and protective upto certain point. Beyond that point, a variety of dysfunctions accompany LVH including lower coronary vasodilatory capacity, depressed left ventricular wall mechanics and abnormal left ventricular diastolic filling pattern. LVH is identified by ECG in only 5 – 10% of hypertensive patients. LVH is found by echocardiography in nearly 30% of unselected hypertensive adults and upto 90% of persons with severe hypertension.

Heart failure:

The various alterations in systolic and diastolic function seen with LVH obviously can progress to congestive cardiac failure (CCF). A 20mm Hg increment in systolic BP conferred a 56% increased risk for CCF in Framingham Cohort. For many undertreated or untreated Hypertensives, LVH is an important intermediate step resulting in Hypertensive heart disease with impaired LV filling and increased ventricular stiffness. This type of heart failure (seen in 40% of hospitalized patients with antecedent history of hypertension) is called Diastolic Dysfunction. The more common type of "Systolic Dysfunction" associated with a reduced LV ejection fraction most often is due to previous myocardial infarction. (For which HT also is an important risk factor).

Coronary artery disease:

Hypertension is a major risk factor for myocardial infarction and ischemia. Prevalence of silent MI is significantly increased in hypertensive subjects and they have a greater risk for mortality after an initial myocardial infarction[2].

Once MI occurs, prognosis is affected by both the pre existing and subsequent BP. An increase in post – MI mortality has been noted among those whose blood pressure fell significantly, presumably a reflection of poor pump

function. If the blood pressure of these subjects remained elevated, the prognosis was even worse, like representing a severe load on the damaged myocardium.

Renal Function :

Both structural damage and functional derangement reflecting intraglomerular hypertension often reflected by microalbumiuria can be found in most hypertensive patients. Microalbuminuria in hypertensive patients has been correlated with LVH and corotid artery thickness. As hypertension induced nephrosclerosis proceeds, plasma creatinine levels begin to rise and eventually renal insufficiency may develop. Any agent or group of agents that adequately lowers BP to levels < 130/85 mm Hg will slow the progression of nephropathy.

Cerebral involvement:

Hypertension may accelerate cognitive decline with age. Hypertension, particularly systolic is a major risk factor for both ischemic stroke and intracerebral haemorrhage. Cerebral white matter lesions are a common finding by brain MRI seen in 41% of asymptomatic, middle aged hypertensive patients than in normotensive subjects.

Evaluation Of A Hypertensive Patient: (JNC 7 recommendations)

Physical examination:

Appropriate measurement of BP, verification in the contralateral arm, examination of optic fundi, body mass index calculated as weight in kilograms divided by square of height in metres (Measurement of waist circumference also may be useful). Also,auscultation for carotid, abdominal and femoral bruit, palpation of thyroid gland, thorough examination of cardiovascular and respiratory system, examination of abdomen for enlarged kidney, masses and abdominal aortic pulsations., palpations of lower extremities for oedema and pulses and a thorough neurological assessment. is important.

Laboratory tests and other diagnostic procedures

Basic tests:

I. Always Included:

1. Urine analysis: Protein, Blood, Glucose, Microscopy
2. Haematocrit
3. Blood glucose
4. S. Creatinine and / or BUN

5. Lipid profile (after 9 – 12 hr fast) – that includes HDL – Cholesterol, LDL – Cholesterol, Triglycerides.
6. Electrocardiogram

European society of HT – European Society of Cardiology also include the following investigations:

Optimal tests:

1. Urine analysis excretion or albumin creatinine ratio. More extensive testing for identifiable causes is not indicated generally unless BP control is not achieved.
2. WBC Count,
3. Serum Phosphate
4. Chest X – ray.
5. Echocardiogram.

More extensive testing for identifiable causes is not indicated generally unless BP control is not achieved.

Hence it is evident that urine albumin excretion is one important parameter which should ideally be included in the evaluation of a hypertensive patient.

MICROALBUMINURIA

Concepts and definition:

Microalbuminuria is defined as UAER of approximately 30 – 300 mg/d (24 hour urine albumin excretion rate) in a samples of nonketonic sterile urine [34-39]. Ideal is the first voided, mid stream morning sample (5ml sample).

ADA and NKF (American Diabetes Association and National Kidney Foudation) define microalbuminuria as an albumin creatinine ratio between 30 – 300 μg/mg in both men and women[7]. Sex specific ACR cutpoints: > 17 μg/mg in men, >25 μg/mg in women.

24 hour urine albumin excretion rate: 30 – 300 mg/d.

Overnight urine albumin excretion rates: 20 - 200μg/hr.

Albumin creatinine ratio : 2.5 – 25mg/mmol (for men) or

3.5– 25 mg/mmol (for women)

30 - 300μg/ mg in both men and women.

The 24 hour urine collection is considered to be the gold standard for assessing the low levels of UAER.The above values,though generally accepted, have been questioned by some authors .[40-43]

Techniques of measurement and monitoring:

Timed urine collections 24 hor or overnight remain the gold standard.

Disadvantage

This is cumbersome to the patient, in repeated large scale screening, this may become a significant problem. For large scale screening use of albumin creatinine ratio in early morning urine is a convenient and reliable screening method.

Potential confounders:

Potential confounders in the detection of microalbuminuria are :

Day – to –day variation of 40%.

False positives:

Strenuous exercise, urinary tract infection, renal disease.[45-47]

Dipsticks exclusively detect albumin, sensitivity being for concentrations as low as 250 mg/ml. .Urine albumin cretatinine ratio can be used in random urine samples. Measurements correlate well with those obtained by classical way. Urine albumin estimated by ELISA or immunoturbidometry and creatinine by Jaffe reaction ,

(rate blanked) , RIA and Nephelometry.

Methods for detecting and measuring proteinuria

Method	Description	Coments
Turbidimetric	Addition of Trichloroacetic or sulfosalicylic acids after colloid properties and produce turbidity to be read in densitometer (Benzathonium chloride also used)	Imprecise, different readings for albumin and globulin
Stick tests	Impregnated with indicator dye (bromocresol green) which changes colour in presence or protein.	Reacts poorly with globulin. Usual clinical screening test.
Nephelometric	Specific anti albumin antibody used.	Measures albumin excretion, not total protein.

Factors that Microalbuminuira helps to predict:

Diabetic renal disease

Diabetic Retinopathy

Complications in pregnancy

Cardiovascular mortality and morbidity in

1. Type I diabetes
2. Type II Diabetes
3. Elderly Non diabetic people
4. Non diabetic people with hypertension

Microalbuminuria in Essential Hypertension.

Microalbuminuria is found in a significant proportion of non diabetic population, particularly in association with essential hypertension, again is predictive of cardiovascular disease.

Epidemiology: Between 2-10% of adult non diabetic population shows persistent microalbuminuria, with higher frequency in certain ethnic groups. . Both microalbuminuria and overt proteinuria are associated with an increase in left ventricular mass, myocardial ischaemia, carotid artery thickness, overall cardiovascular morbidity and mortality[6].

Association of Microalbuminuria with other cardiovascular risk factors:

Microalbuminuria and Hypertension

Patients with HT who show excess protein leakage tend to have greater evidence of cardiovascular comorbidities such as dyslipidemia and glucose intolerance, plus higher left ventricular mass, greater risk of hypertensive retinopathy and evidence of increased and more progressive atherosclerosis. A raised UAE rate during acute MI is also predictive of inhospital mortality and is independent of other systemic markers.

Mechanisms of Association between microalbuminuria and hypertension: 3 mechanisms are described

1. Increased intraglomerular pressure [48]
2. Intrinsic glomerular damage causing changes in glomerular filtration barrier [50,51]
3. Tubular dysfunction resulting in prevention of normal reabsorption of filtered albumin.

Microalbuminuria and Hypertension – Implications for treatment

Studies in essential hypertensives with microalbuminuria have shown that ACEI have a greater capacity to decrease microalbuminuria than other group of antihypertensives. ARBs may show similar benefits from the point of view of renal microcirculation[6].

Role of ACEI Drugs:

Most studies have reported greater reduction in UAE rates in patients with hypertension with microalbuminuria using ACE inhibitors compared with other antihypertensive drugs such as β blockers, α Blockers and CCBs. The reason for the apparent advantage of ACEI over other classes may relate to specific effects on

the renal microcirculation thereby reducing intraglomerular pressure and protein leakage.

What is not clear is whether reduction in UAE rates in patients with essential hypertension relates to long term renal and more importantly cardiovascular protection. This issue was addressed in part by HOPE study. A randomized Control Trial of over 9000 patients at high cardiovascular risk – they were either diabetic (around 35000 patients) or non diabetic with a previous vascular event. They were randomized to receive ACEI , Ramipril or placebo and followed for five years. During the study they could have any other treatment including antihypertensives. There was clear separation in the composite end point of cardiovascular mortality, MI and stroke, and also in each of these variables independently in favour of ACEI. There was also evidence for renal protection in the diabetic subgroup. They also demonstrated cardiovascular protection with ACEI. But the HOPE study did not specifically look at the relationship between mircoalbuminuria and cardiovascular risk and whether improvement in microalbuminuria will reduce that risk. The evidence for ACE inhibition being cardiovascular protective is also supported by recent data from the Perindopril Protection Against Recurrent Stroke Study (PROGRESS) using ACEI Perindopril.

Angiotensin II receptor Blockers:

Recently few studies have been published which report renal protection by using ARBs from the point of view of further progression of overt nephropathy or conversion from incipient to overt nephropathy. Data in non diabetic population is limited. A study comparing ARB Losartan and Enalapril showed that the former reduced mircoalbuminuria as affectively as the latter. To date, there is no evidence of cardio protection with these agents.

LEFT VETNRICULAR HYPERTROPHY

Electrocardiography

Sokolow – lyon index: $SV_1 + (RV_5 – \text{or } RV_6) > 3.5mv$. R avL > 1.1mv.

Romhilt Estes Point score system :

Any limb lead R wave or S wave $\geq$ 2.0mv	3 points
or SV_1 or $SV_2 \geq$ 3.0mV	3 points
or RV_5 or $RV_6 \geq$ 3.0mV	3 points
ST – T wave abnormalities (no digitalis)	3 points
ST – T wave abnormalities (digitalis therapy)	1 point
Left Atrial abnormality	3 points
Left Axis Deviation ($\geq 30^o$)	2 points
QRS duration $\geq$ 90 msec	1 point
Intrinsicoid deflection in V_5 or $V_6 \geq$ 50msec	1 point

A score of 5 points is considered as LVH.

ECHOCARDIOGRAPHY

Hypertensive heart disease is characterized by concentric left ventricular hypertrophy with increased wall thickness and non dilated chamber. Hypertrophy is symmetric. LV mass can be calculated from M mode data. LV mass is the total weight of myocardium.

Dimensions needed : ST – Septal thickness (0.6 – 1.1)

PWT – Posterior wall thickness (0.6 – 1.1)

LVID - Left ventricular internal dimension at end diastole.

$$\text{LV Mass} = 0.80 \text{ X } [1.04 (ST + PWT + LVID)^3 – LVID^3] + 0.6g$$

$$\text{Relative wall thickness} = \frac{\text{Septal wall thickness + Posterior wall thickness}}{\text{LV end diastolic diameter}}$$

HYPERTENSIVE HEART DISEASE

Left ventricular hypertrophy,

Diastolic Dysfunction, systolic dysfunction (Long standing cases)

Aortic root dilatation

Aortic valve sclerosis,

Mitral Annnular calcification

LA enlargement;

Atrial Fibrillation.

Classification of Diastolic Dysfunction.

Pathophysiology	Normal	Mild	Mild-Moderate	Moderate	Severe
		↓ Relaxation	↓ Relaxation ↑ LVEDP	↓ relaxation ↓ Compliance ↑ LVEDP	↓ Relaxation ↓↓ Compliance ↑↑ LVEDP
E/A Ratio	1 – 2	< 1	< 1	1 – 2	> 2
IVRT msec	50-100	> 100	Normal	↓	↓
DT msec	150-200	> 200	> 200	150-200	< 150
E/A Ratio = Ratio of early to atrial transmitral velocity IVRT – Isovolumetric relxation time DT = Deceleration time of pulmonary venous diastolic flow phase					

Diastolic Function:

Diastolic dysfunction in hypertension is characterized by:

Impaired early diastolic relaxation, prolonged Isovolumic Relaxation Time (IVRT); Reduced E velocity, Reduced E/A ratio, Prolonged Deceleration slope.

Systolic function

Preserved early in the course of disease

Segmental wall motion abnormalities are not seen unless co existing CAD is present.

Assessment of LV systolic function

1. Ventricular Volumes & Geometry, End Diastolic Volume (EDV) & End systolic volume (ESV) are measured (LVID or LV internal dimensions).

Ejection Fraction (EF) = $\frac{SV}{EDV}$ X 100. Where SV = Stroke volume(SV = EDV-ESV)

2. LV mass : is derived by multiplying the volume of myocardium times the specific density of cardiac muscle
3. Fraction shortening (%) : N = Normal = 25 – 45%

$$\frac{LVIDd - LVIDs}{LVIDd} \times 100$$

4. LV wall stress : Calculated by Relative Wall thickness (RWT)

$RWT = \frac{2 \times PWT}{LVID}$ PWT = Posterior Wall thickness
LVID = LV internal dimensions.

An overview of the previous studies on this area:

Results of large epidemiological studies have demonstrated that regardless of the severity of hypertension, the cost effectiveness of BP reduction by drug therapy is greater in presence of target organ abnormalities and/or comorbidities. In this context, assessment of subclinical organ damage namely LVH & peripheral atherosclerosis has become a key element in evaluating hypertensive patients.

In a study conducted in department of Internal Medicine, University of Genova, Italy, consisting of 279 patients, microalbuminuric patients were 21 times more likely to have both LVH and increased carotid IMT ($P < 0.0001$) as

compared with those with normal albumin excretion. In another study Berton et al showed that the presence of microalbuminuria strongly predicts mortality in patients with acute myocardial infarction even after adjusting all other confounders. Increased UAE has also been related to peripheral atherosclerosis and increased carotid intima – media thickness (IMT). In line with these findings, another preliminary study has found increased prevalence of asymptomatic cerebral vascular lesions as evidenced by NMR imaging in Hypertensive patients with microalbuminuria as compared with a group of well matched hypertensives with normal albuminuria. Increased BP load and variability, higher uric acid levels, worse lipid profiles, Insulin resistance, Endothelial dysfunction, increased activity of RAAS[18,19].

Microalbuminuria possibly reflects a state of increased renal endothelial permeability and may be an easily measured marker of rather diffuse endothelial dysfunction, low grade inflammation and vascular disease burden.During 10years significant no. of scientific contributions have shown that increased UAER

constitutes and independent predictor of atherosclerotic cardiovascular disease in non diabetic subjects, in elderly, in general population as well as in hypertensive patients In addition, evaluation of UAER is one of the recommended laboratory tests proposed by European Society of Hypertension guidelines to assess target organ damage in Hypertensive subjects[29].

The first report on the association between microalbuminuria and increased risk of cardiovascular events in non diabetic subjects was published in 1988. In Hoorn study, the relative risk of all cause mortality associated with microalbuminuria and peripheral arterial disease was about 5 times higher among hypertensive than normotensive subjects In the prevention of Renal and Vascular End stage disease study, microalbuminuria in addition to conventional cardiovascular risk indicators was independently associated with ischemic electrocardiographic abnormalities reflecting underlying coronary artery disease[29].

Interestingly, in a cohort of elderly hypertensive individuals without previous cardiovascular complications, augmented UAER was predictor of adverse cardiovascular events, irrespective of BP levels. In a group of subjects during the first week after an acute ischemic event, elevated UAER proved to be a significant predictor of 1year mortality, independent of the other cardiovascular risk factors. Even minimal increments of UAER could be clinically significant in hypertensive patients. In HOPE study (Heart Outcomes Prevention Evaluation Study) with a median of 4.5 years of follow up, any degree of mciroalbuminuria was proven to be a risk factor for cardiovascular events in individuals with or without diabetes. The risk increases with the urine albumin creatinine ratio; starting well below the microalbuminuria cut off; even as low as 0.5mg/mmol. For every 0.4mg/mmol increase in albumin – to – creatinine ratio, the adjusted hazard of major

cardiovascular events augmented by 5.9%. Albumin creatinine ratio of >0.65mg/mol was associated with augmented risk of developing fatal and non fatal ischemic heart disease. In the light of most recent data from the LIFE study (Losartan Intervention for Endpoint Reduction Study) in non diabetic hypertensives with LV hypertrophy, the risk of cardiovascular morbidity and mortality increased continuously as UAER augmented, without thresholds or plateaus (Gerstein et al 2001). Based on the above, there is probably a necessity of shifting downward the limits for diagnosing microalbuminuria in Essential HT, starting well below the conventional cut off.

At present LV hypertrophy is considered as potent marker of cardiovascular risk and an important surrogate end point in Essential hypertension. According to several cross sectional studies, either by ECG or echocardiography, microalbuminuric patients exhibited a higher prevalence of LVH compared to normal albuminurics. Vast majority of the reports supported the view that hypertensives with elevated UAER had higher LV mass index; indicating that renal damage and LV hypertrophy are parallel phenomena. Microalbuminuria is accompanied by concentric type of LV hypertrophy – LV condition with most adverse cardiovascular outcome. Microalbuminuria has also been related, independent of the BP levels and LV mass with preclinical impairment of LV diastolic function; strengthening its role as a marker of early cardiac involvement

in hypertensive populations. A late study in 330 never treated non diabetic, hypertensives, showed a robust, graded, pressure independent link between increasing LV mass index and augmented UAER (Di Bello et al, 2003). The proposed cause for an elevated UAER in hypertensive patients with LVH is the increased levels of ANP secreted from the hypertrophied ventricles. The fact that subjects with heart failure and elevated ANP levels exhibit microalbuminuria further supports this view.

Hypertension induced structural and functional modification of large arteries may be directly related to the well recognized complication of Essential hypertension involving CNS, heart and kidneys. The intima – media thickness of the carotid artery and the existence of atherosclerotic plaques and correlated to several cardiovascular risk factors and to the incidence of cardiovascular disease. Microalbuminuric subjects exhibit increased carotid artery wall intima – media thickness (IMT), higher frequency of plaques in arterial segments compared to normoalbuminuric subjects (Trepstar et al 2002) . Arterial stiffness, the major determinant of central pulse pressure may be an independent marker of cardiovascular risk in Essential Hypertension. High pulse pressure is closely associated with increase in urine albumin excretion rate. Hypertensive patients with microalbuminuria have earlier systolic augmentation in carotid arterial

pressure contour, reflecting increased arterial stiffness – this was proven in a study conducted in 162 hypertensive patients (Lambraou et al 2000).

Renal damage and microalbuminuria

Microalbuminuria may be a predictor of progressive deterioration of renal function – as shown by some preliminary studies. In a few studies that examined the issue of relationship of microalbuminuria with increased risk of renal dysfunction, independent of BP levels and smoking habits, the results are rather conflicting. More specifically, in one study, greater decline in renal function was observed in hypertensive subjects with microalbuminuria, where as other investigators found that increased renal albumin excretion rate has no renal prognostic significance.

The association of microalbuminuria with augmented cardiovascular risk may be explained at least partially by the frequent co existence of elevated UAER with a series of well established markers of cardiovascular risk such as dyslipidemia, non diabetic hyperglycemia, higher Body Mass Index, Central obesity; high serum uric acid; increased salt sensitivity, hyperhomocystinemia; dietary protein, smoking, sedentary life style, family history of essential hypertension, increased pulse pressure and absence of nocturnal BP decrease.(Garg et al 2002).

The role of inflammatory process as one of the pathophysiological links of microalbuminuria with high cardiovascular states cannot be ruled out. Elevated UAER is related to chronic low grade inflammation, the latter is closely associated with unfavourable cardiovascular outcome and atherosclerosis, mediating all stages of atherosclerotic vascular disease form initiation to progression and ultimately thrombotic complications. Significant graded relationship between BP and levels of inflammatory markers (IL – 6 and soluble ICAM – 1) were observed in healthy subjects. Increased levels of vascular cell Adhesion molecule – 1 (VCAM – 1), CRP and fibrinogen are related to augmented UAER in diabetic and non diabetic subjects (Pannaciulli et al, 2001). In certain cohorts, higher amounts of VCAM – 1 and CRP are related to microalbuminuria, more strongly in non diabetics than diabetics. There was also positive relation with microalbuminuira, levels of diastolic BP and CRP levels in a study in which diabetic patients were excluded. Till now there are no data from a trial with only hypertensive subjects participating in it, there is cumulative evidence to support a possible relationship of microalbuminuria with markers of subclinical inflammation in the setting of essential HT. (Jager et al, 2002).

. In a relatively small retrospective study, microalbuminuria predicted subsequent loss of renal function, despite similar baseline clinical characteristics and current BP levels through the study period (Bigazzi et al, 1998). More

recently, provocative data from a large cross sectional study indicate that high normal albuminuria (between 15 – 30mg/day) is associated with hyperfiltration in glomeruli (similar to diabetes), it could anticipate a decline in renal function (Veglio F et al, 1992). In conclusion, although well conducted large prospective studies addressing this issue are yet to be carried out, the predictive value of microalbuminuria for hypertension – induced renal damage is at present a tempting, but speculative hypothesis[8].

Preserving cardiac function in hypertensive patient - importance of renal parameters.

Hypertensive cardiovascular disease is a systemic condition with potentially devastating long term effects on vascular and end organ function. Although the foremost object of cardiologists concerned with its management is to protect patients against cardiac events and stroke, renal dysfunction is an integral component of the disease and a highly sensitive and predictive marker of its progress. It is therefore surprising that, despite enormous diagnostic and therapeutic potential, renal considerations are still under utilized by cardiologists in the routine management of hypertension.

Despite being readily available and amenable to intervention, renal parameters are under exploited in two key ways. Microalbuminuria measurement has yet to become routine for hypertensives, either within the clinic or in the

general practice setting. It is a highly sensitive, readily assessed marker of incipient nephropathy and systemic endothelial pathology. It is an independent predictor of either renal failure or cardiovascular morbidity and mortality. Therefore, its measurement should be incorporated within standard management protocols for all patients with hypertension or diabetes.

Sustained renal function should be a key goal of therapeutic intervention in early – stage disease for cardiologists as well as nephrologists. Agents that delay the progression of renal disease are likely to protect against adverse cardiovascular outcomes by protecting against the systemic consequences of renal disease and in addition, may exert beneficial effects on endothelia throughout the vasculature and in the heart.

The relationship between renal and wider cardiovascular diseases is most evident in their advanced stages. About half of the patients with congestive heart failure have chronic kidney disease, whereas congestive heart failure is about 15 times more common in patients with chronic kidney disease than in patients with normal renal function. Congestive heart failure exacerbates nephropathy, whereas chronic kidney disease is associated with accelerated atherosclerosis, microvessel disease, endothelial dysfunction, and increased sympathetic activity and cardiac pathology. Renal artery stenosis and renovascular hypertension may also impact both on the non stenotic kidney and the heart.

At the early stages of disease, when a patient may present with few overt pathologies other than hypertension, the relationship between renal and cardiovascular pathologies is also predictive of long term outcome and is more amenable to successful long term intervention. Vascular, cerebrovascular, and coronary diseases, ventricular hypertrophy, and ultimately, nephropathy and heart failure are all potential endpoints of a broad syndrome that is symptomatically silent for many years and involves a network of interlocked disease processes, which include sympathetic activation, haemodynamic changes, insulin resistance, inflammatory processes, dyslipidaemia, dysregulation of cytokines and growth factors, and consequent to many of these processes, endothelial damage. One of the critical driving factors of this network is increased activity of the rennin angiotensin aldosterone system (RAAS), both within the kidney and vascular endothelium. One the basis of this pathophysiological role, it has been posited that RAAS blockade may provide a promising strategy for early therapeutic intervention in hypertensives with renal or atherosclerotic disease.

There is abundant evidence that the occurrence of microalbuminuria in patients with hypertension or diabetes predicts adverse outcome. The LIFE (Losartan Intevention For Endpoint reduction in hypertension) study in high risk hypertensives found that increased urinary albumin excretion is associated with left ventricular hypertrophy, abnormal geometry, and increased ventricular mass. The

association was independent of blood pressure, diabetes, serum creatinine, age, or race, suggesting a close and direct correspondence between albuminuria and cardiac damage. In the Heart Outcomes Prevention Evaluation (HOPE) Study, every 0.4mg/mmol/L increase in albumin: creatinine ratio increased the adjusted hazard for major cardiovascular events by 5.9%. Recently, the Prevention of Renal and Vascular End stage Disease (PREVEND) study demonstrated that fosinopril treatment vs. pravastatin significantly lowered urinary albumin excretion in patients with microalbuminuria and correspondingly was associated with a 40% (P = 0.098) reduction in cardiovascular events. Although this study did not enable the beneficial effects of reduced blood pressure per se and RAAS specific actions independent of blood pressure reduction to be distinguished, it is suggestive of a relationship between microalbuminuria and cardiovascular events.

Thus,it is not surprising that microalbuminuria was found to be an excellent predictor of cardiovascular morbidity and mortality in subjects with and without hypertension, in several prospective studies [31,32,33].

From renoprotection to cardioprotection: the emerging role of RAAS blockade

Since renal dysfunction is now known to be a core driver of cardiovascular pathology even at the earliest stages of hypertensive disease, interventions that delay or reverse the development of nephropathy should be integrated in the

management of hypertension whenever microalbuminuria or frank proteinuiria are detected. All agents that reduce systolic and diastolic blood pressures reduce albuminuria, but the most potent renoprotective drugs appear to be antihypertensive agents which block the RAAS. These agents selectively attenuate intra glomerular pressure by promoting vasodilatation of the glomerular efferent arterioles and favourably affect the regression remodeling and the improvement of endothelial function in resistance arterioles, particularly in patients with nephrosclerosis. A number of angiotensin converting enzyme (ACE) inhibitors and two angiotensin II receptor blockers (ARBs) irbesartan and losartan, have demonstrated renoprotective effects in major prospective trials. New classes of agents, such as rennin inhibitors and selective aldosterone receptor antagonists, also have renoprotective potential, although these agents currently lack the support of large clinical trials data available for some ARBs and ACE-inhibitors. Further studies will be needed to characterize the most appropriate strategy using RAAS blockade across the spectrum from early to large – stage kidney disease.

MATERIALS AND METHODS

Study type : Descriptive study

Population: Adult Systemic hypertension patients (inpatients/outpatients) , Department of General Medicine, Coimbatore Medical College Hospital.

Duration : January 2008 to August 2009.

Inclusion criteria : Patients with Systemic Hypertension {as defined by The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)} admitted in General Medicine wards or Outpatients, not having any of the exclusion criteria**.**

Exclusion criteria: Pregnant women ,those with diabetes mellitus(also impaired fasting glucose and impaired glucose tolerance),renal disease, urinary tract infection, raised blood urea and serum creatinine and macroproteinuria (albumin excretion more than 300 mg/24 hours), were excluded from the study

Methodology : Each participant was interviewed and examined in detail.

1. History of hypertension given by the patients or relatives which was verified with previous records – OP tickets, or discharge cards. History of treatment for hypertension was also included.

2. Newly detected Hypertensives: Hypertension was diagnosed on the basis of the BP recorded in the arms with Mercury Sphygmomanometer: Office measurements were used for OP patients. For out patients, three recordings one week apart were used. For inpatients, two recordings during the IP treatment period & one during their first review in OP were taken. On each occasion, two readings were taken. BP was taken with and the patient sitting relaxed, back supported, for five minutes and arm supported at the level of heart. All the recordings greater than 140/90mm Hg were regarded as Hypertension, which was confirmed at other occasions as mentioned above.
3. A detailed case record was prepared for each patient on the basis of specially designed proforma. The important factors considered in history were: the duration of hypertension and treatment; history of smoking; symptoms pertaining to cardiovascular and nervous system which could possibly suggest a target organ damage.
4. Neurological symptoms considered were headache, seizure, altered sensorium, focal deficits or stroke. Cardiovascular symptoms considered were dyspnoea, palpitation and chest pain. The duration of Hypertension was an important concern. Hence the study population was divided into four groups:
    1. Less than 1 year
    2. 1 to 5 years since diagnosis

3. 5 -10 years since diagnosis
4. >10years since diagnosis- long duration

This was an arbitrary division done for the ease of comparison.

Based on the level of BP, the patients were divided into 3 groups as follows:

1. Less than 140/90 mm Hg. (Adequate control with drug therapy)
2. Systolic BP: 140 – 159 mm Hg

   Diastolic BP : 90 – 99 mm Hg - Stage I of JNC 7 report
3. Systolic BP : >160 mm Hg

   Diastolic BP : >100 – 109 mm Hg Stage II of JNC 7 report

Body mass index:

Weight and height was measured for all ambulant patients and BMI expressed in Kg/m^2. Based on BMI, the study group was classified into:

Under weight : <18.5
Normal : 18.5 – 24.9
Over weight : 25.0 – 29.9
Obese : 30 – 39.9
Extremely obese : >40

Examination of all organ systems were done, with special emphasis on nervous system for any evidence of stroke and cardiovascular system for cardiomegaly or evidence of systolic or diastolic dysfunction of heart.

Fundus Examination: Done by direct ophthalmoscopy; pupillary dilatation achieved using 1% Tropicamide. According to Fundus findings, the patients were divided into 6 groups. (Refer to Review of Literature):

1. Fundus normal
2. Fundus not visualized (Due to hazy media)
3. Grade I Hypertensive Retinopathy
4. Grade II Hypertensive Retinopathy
5. Grade.III Hypertensive Retinopathy
6. Grade. IV Hypertensive Retinopathy

Keith – Wagener Barker Classification

Investigations done included:

Random blood sugar,fasting and post prondial blood sugar was done in all patients to exclude diabetes.

Serum creatinine and blood urea– Only those patients with normal value were taken up for the study.

Urine examination – Albumin, RBC, WBC, Bacteria, Urine culture, ketones. Only those patients with normal urine examination results were included.

Lipid profile (Fasting): Was done for all patients. They were divided into two groups.

a. Favorable lipid profile

b. Unfavorable lipid profile

(Based on the LDL – C, HDL – C, TG and total cholesterol values)

The CHD risk was assessed on the basis of the ATP III guidelines of NCEP and the patients classified into different risk groups. LDL –C of the patients were compared with that of the goal set for each risk group to determine whether the lipid profile was favourable or unfavourable.

Electrocardiogram: was taken for all patients to look for LVH. The Sokolow – Lyon Index and the Romhilt – Estes point score system were used to diagnose LVH. The patients satisfying the criteria of either of these were considered as having LVH. The two criteria were used together because of the low sensitivity of either of them taken alone (10 – 30%).

Chest X – ray: was taken in all patients to look for cardiomegaly. If the transverse dimension of the cardiac shadow exceeded 50% of that of the thorax, it was taken as cardiomegaly.

CT Brain: was taken for all patients admitted with a clinical diagnosis of Stroke/ seizure/ or altered sensorium.

Cardiac enzymes /Treadmill test as indicated for diagnosis of Coronary artery disease

Echocardiogram: Done to assesstwo dimensional guided M-mode echocardiography was performed at the parasternal long axis view and apex;

LVID at end systole & end diastole as well as IV septum and posterior wall thickness were assessed in accordance to the recommendations of American Society of echocardiography.

1. LV Geometry → LVH present or not; based on the LV mass and relative wall thickness determined by M mode ECHO. Normal upper limit of LV mass (absolute value). Men – 259 g; Women – 166g.Concentric LV Hypertrophy was considered present if Relative wall thickness was > 0.43 OR LV Mass was increased.
2. LV function: LV systolic/ diastolic dysfunction – were assessed on the basis of parameters mentioned previously.
3. Chambers, valves, flow and regional wall motion were assessed.
4. Wall motion abnormalities.

Microalbuminuria:: Aassessed by spot urine albumin: creatinine ratio (ACR) based on the recommendations of National Kidney Foundation and American Diabetic Association 1st voided midstream early morning sample of 5ml urine.

Patients were asked to avoid exercise prior to collection, urine examination done in women in non menstrual phase. Any value in between 30 – 300 μg/mg creatinine was taken as microalbuminuria. The data were analyzed using the program Epi Info® version 6.The chi-square(χ^2) test was used to compare variable prevalence between the groups, using a confidence interval of 95% ($p<0.05$).

RESULTS & ANALYSIS

A total of 100 hypertensive patients were studied.

Table No:1 – Sex Distribution of study group

Sex	No. of patients	Percentage
Male	49	49
Female	51	51

Figure No:1-Sex distribution of study group

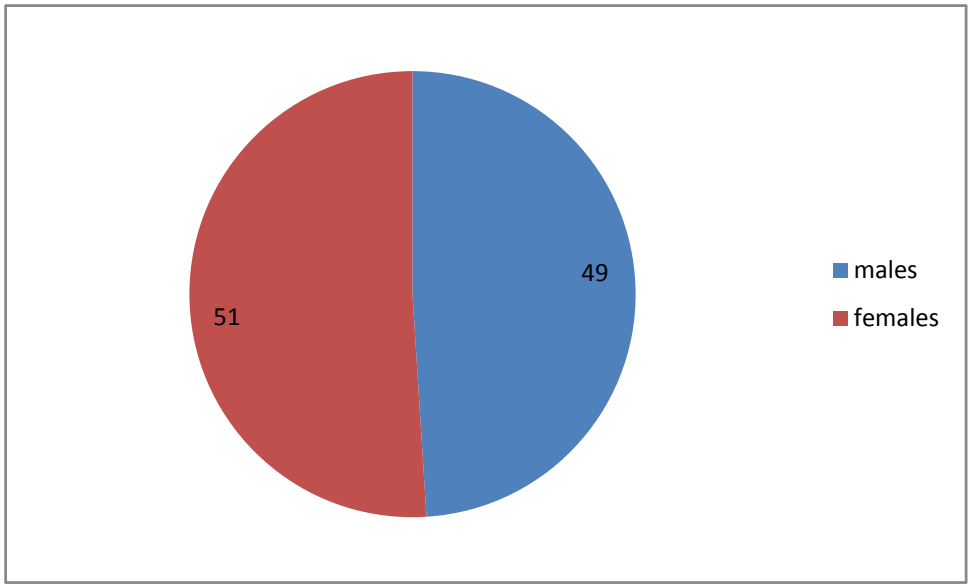
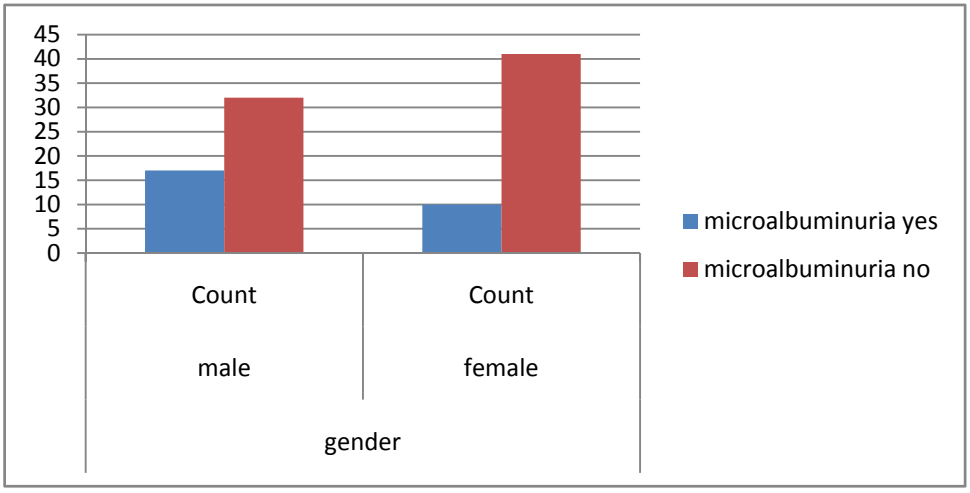


Table No:2 - Distribution of microalbuminuria among males & female

Microalbuminuria	Total No:	Gender				
		Male		Female		
		No.	%		%	
Present	27	17	62.9	10	37.1	p=0.08 χ^2 = 2.89
Absent	73	32	43.8	41	56.2	

Figure No:2 - Distribution of microalbuminuria among males & female



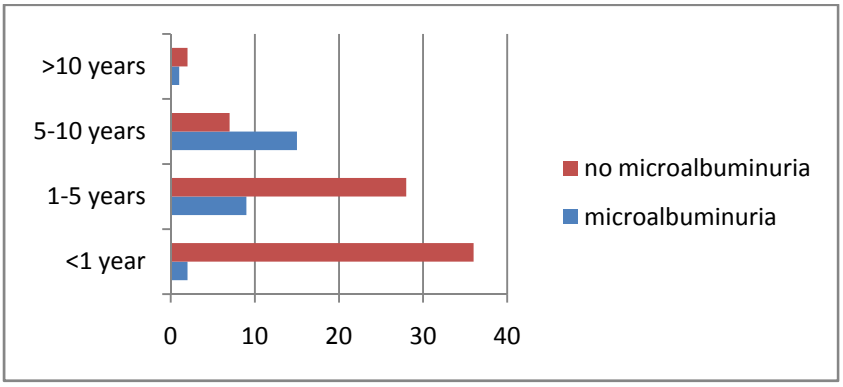
There was no statistically significant difference in the prevalence of microalbuminuria in male & female hypertensives. (p>0.05)

The mean systolic BP among study population was 142.9 mm of Hg while mean Diastolic BP was 88.2 mm of Hg.Relationship of microalbuminuria to duration of hypertension was studied.

Table No:3 – Distribution of microalbuminuria among different groups – depending upon the duration of hypertension

Microalbuminuria	Total No:	Duration of Hypertension(in years)				
		<1	1-5	5-10	>10	p= <0.001 χ^2 =41.2
Present	27	2	9	15	1	
Absent	63	36	28	7	2	

Figure No:3 – Distribution of microalbuminuria among different groups – depending upon the duration of hypertension

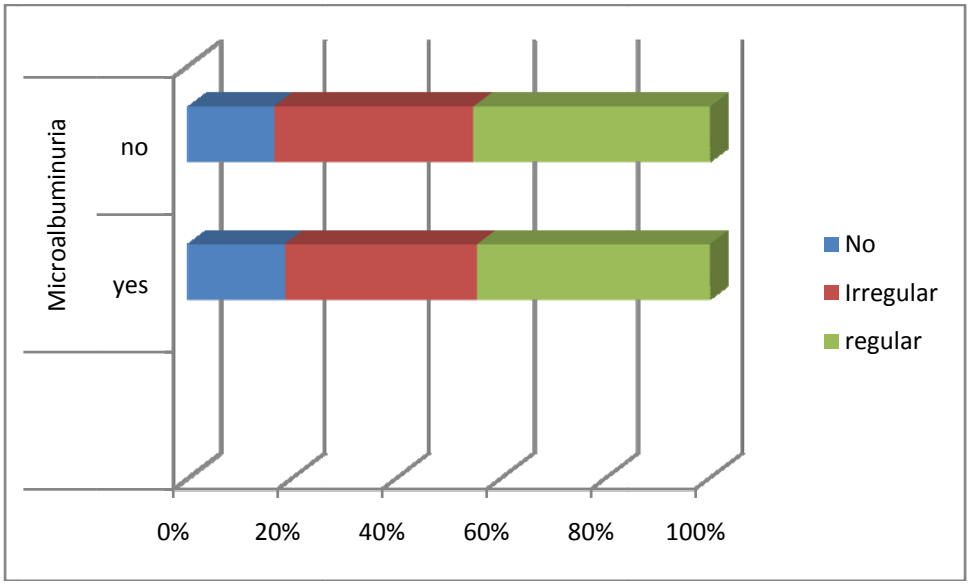


There was statistically significant increase in the prevalence of microalbuminuria among patients with hypertension of long duration. ($p<0.05$)

Table No:4 – Distribution of microalbuminuria among treated and untreated hypertensives

Treatment	Total No:	Microalbuminuria				
		Present		Absent		
		No.	%	No.	%	
No Treatment	17	5	29.4	12	70.6	$p = 0.94$ $\chi^2 = 0.03$
Irregular treatment	38	10	26.3	28	73.7	
Regular treatment	45	12	26.6	33	73.4	

Figure No:4 – Distribution of microalbuminuria among treated and untreated hypertensives

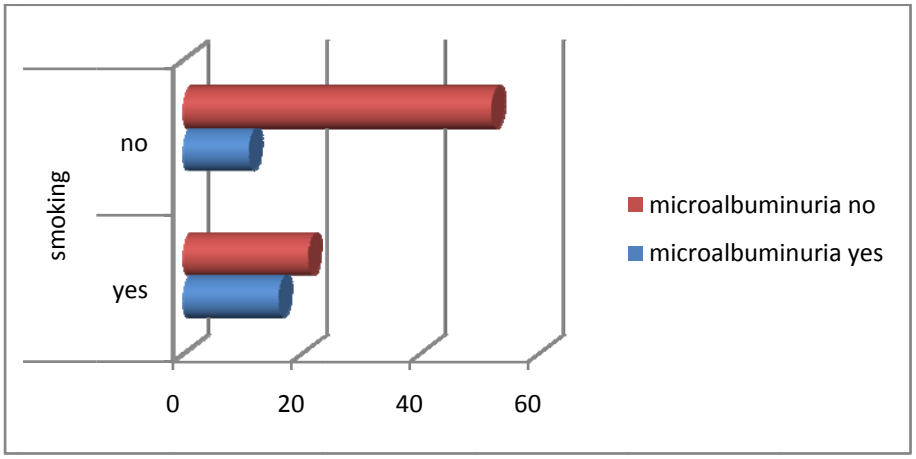


There is no statistically significant difference in microalbuminuria among untreated,irregularly treated and regularly treated hypertensive patients.($p>0.05$)

Table No:5 – Distribution of microalbuminuria among smokers&non smokers

Smoking	Total No:	Microalbuminuria				
		Absent		Present		
		No.	%	No.	%	
Non smoker	6 3	52	82.5	11	17.5	p=0.0050 χ^2 =7.86
Smoker	37	21	56.7	16	43.3	

Figure No:5 – Distribution of microalbuminuria among smokers & non smokers



There was statistically significant difference among the prevalence of microalbuminuria among smokers & non smokers. ($p<0.05$)

Table No:6 – Body mass Index and microalbuminuria

BMI	Total No:	Microalbuminuria		
		Present	Absent	
		No	No	
Normal	71	20	51	
Over weight	20	6	14	P = 0. 714 χ^2 =1.36
Obese	8	1	7	
Extreme obesity	1	0	1	

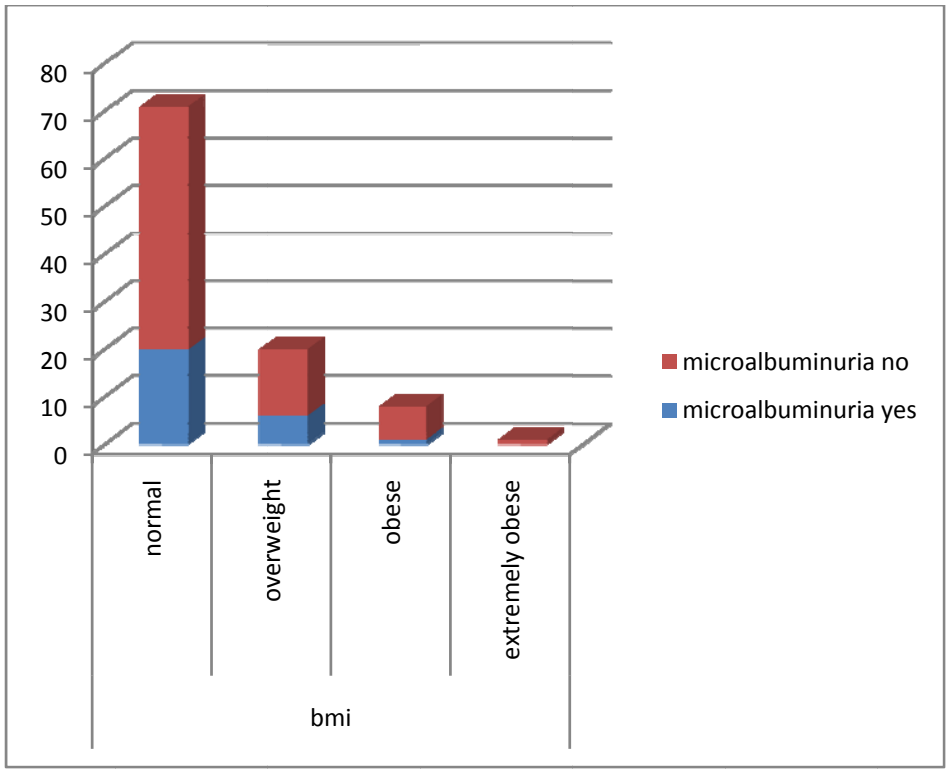


Figure No:6 – Body mass Index and microalbuminuria

The mean BMI of study group was 24.03

Microalbuminuria was found to have no significant association with BMI. ($p>0.05$)

Table No:7 – Lipid profile and microalbuminuria

Lipid profile	Total No:	Microalbuminuria				
		present	%	absent	%	
Favourable	62	14	22.5	48	77.5	p=0.203 χ^2 =1.62
Unfavourable	38	13	34.2	25	65.8	

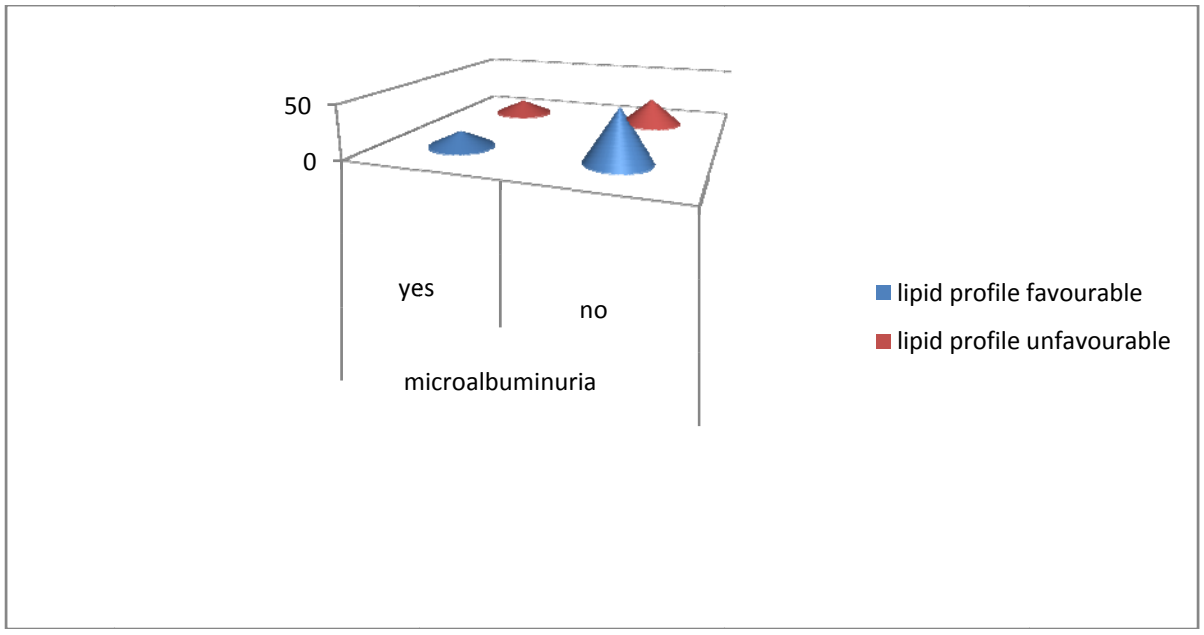


Figure No:7 – Lipid profile and microalbuminuria

The mean total cholesterol in study population was 174.24mg/dl,while triglycerides was 157.72 mg/dl and mean HDL was 47.71mg/dl.

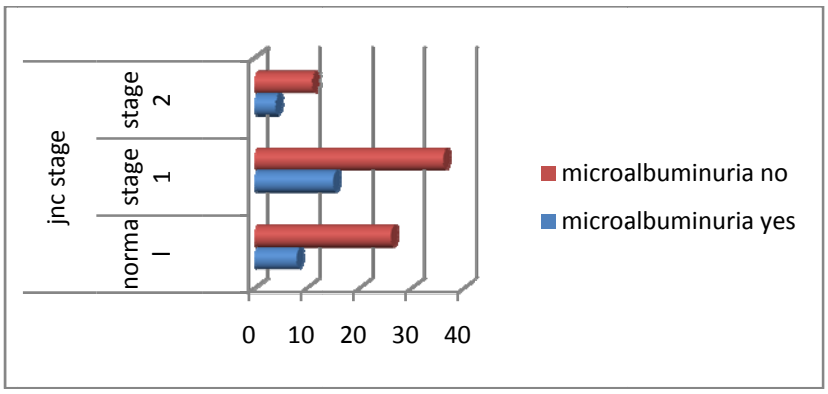
Presence of micoalbuminuria had no relation to lipid profile in this study .($p>0.05$)

Table No:8 – Microalbuminuria & the level of blood pressure

Stage of Hypertension	Total No: of cases	Microalbuminuria				
		present	%	absent	%	
Normal	34	8	23.5	26	76.5	$p = 0.83$ $\chi^2 = 0.36$
Stage I	51	15	29.4	36	70.6	
Stage II	15	4	26.7	11	73.3	

As only confirmed hypertensives are included in the study,those with blood pressure in prehypertensive range as defined by JNC -7,were included in normal group.

Figure No:8 – Microalbuminuria & the level of blood pressure



There was no significant correlation between degree of Hypertension and presence of microalbuminuria.(as p>0.05)

<u>Microalbuminuria and Indices of Target Organ Damage</u>

The indices studied were Hypertensive Retinopathy, stroke and abnormalities in LV geometry (LVH) or LV function and coronary artery disease.

Abnormalities in Fundus Examination:

59 patients had changes of hypertensive retinopathy

27 patients had normal fundus

14 patients – fundus was not visualized due to hazy media

Of the 59 patients with fundus changes

19 patients had microalbuminuria (32.2%)

40 patients did not have microalbuminuria (67.79%)

Table No: 9 –Microalbuminuria and hypertensive retinopathy

Fundus	Total No: of cases	Microalbuminuria				
		Absent		Present		
		No	%	No.	%	
Normal	27	21	77	6	23	p =0. 00008 χ^2 =10.74
Grade I	8	4	50	4	50	
Grade II	34	27	79	7	21	
Grade III	12	7	58	5	42	
Grade IV	5	2	40	3	60	

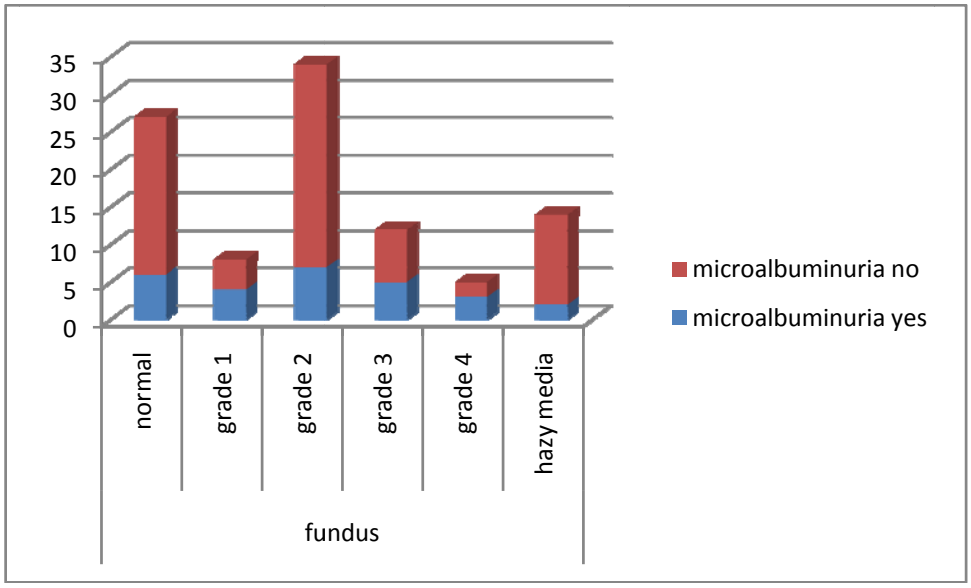


Figure No: 9 –Microalbuminuria and hypertensive retinopathy

Microalbuminuria has statistically significant association with hypertensive retinopathy .($p<0.05$)

Stroke and Microalbuminuria

CT Brain was taken for 26 patients

Indication were : Focal defects in 18 patients

Seizure in 2 patients

Altered sensorium in 6 patients

CT findings:

Normal - 5 patients

Abnormal – 21 patients

Haemorrhage - 5 patients

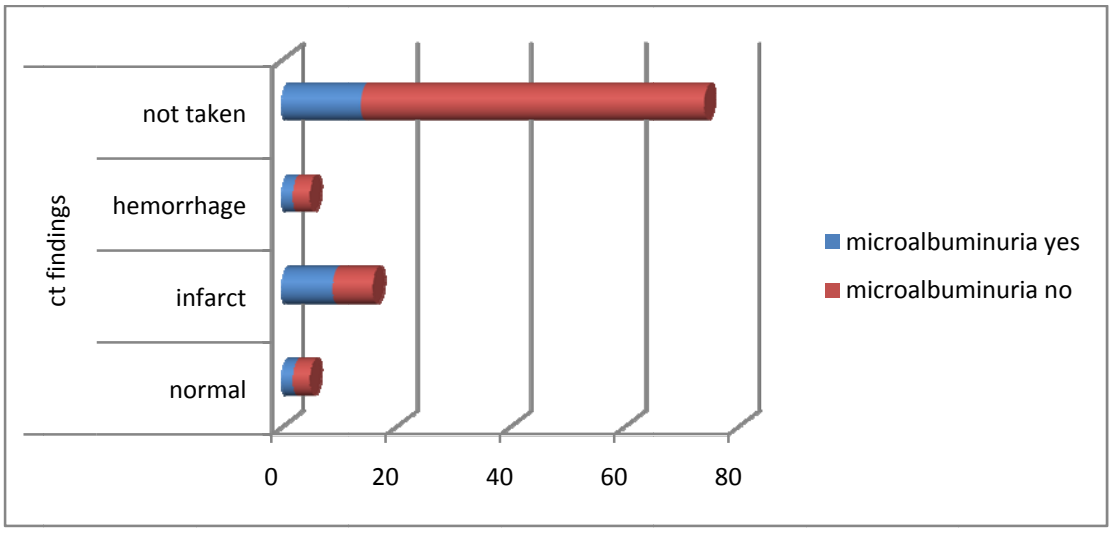
Infarct - 16 patients

CT was not taken in 74 patients as their neurological examination was normal.

Table No:10 –Distribution of Microalbuminuria in CVA

CT brain	Total No: of cases	Microalbuminuria				
		present		absent		
		No	%	No	%	
Normal	5	2	40	3	60	P = 0.61 χ^2 =0.25
Abnormal	21	11	52.3	10	47.7	
Not taken	74	14	18.9	60	81. 1	

Figure No:10 –Distribution of Microalbuminuria in CVA



There is no statistical relation between incidence of microalbuminuria to incidence of CVA in hypertension.($p>0.05$)

Microalbuminuria and hypertensive heart disease

Abnormalities in LV Geometry: Left ventricular hypertrophy [LVH]:

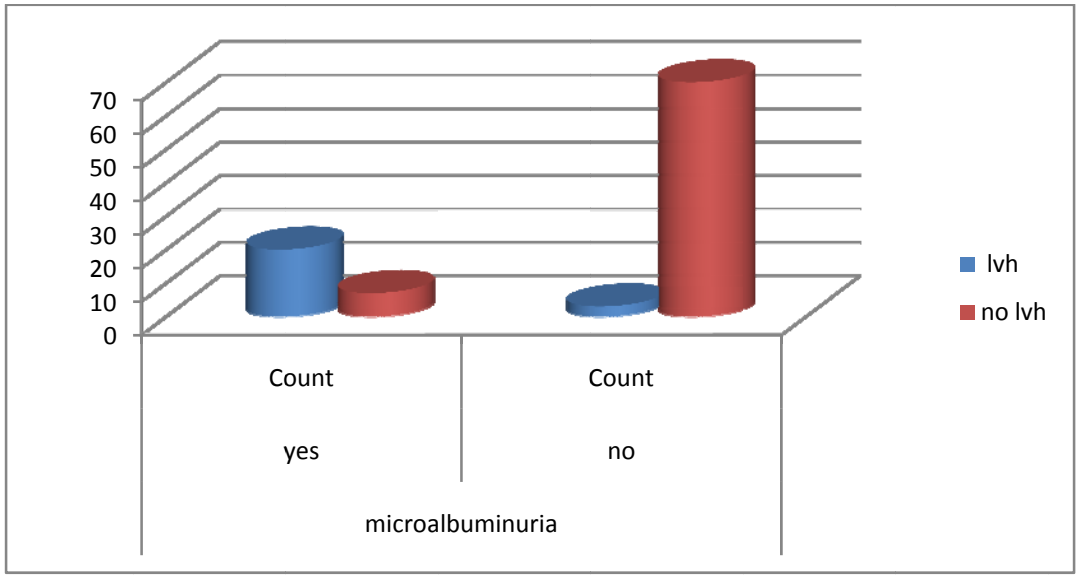
A total of 23 patients out of the 100 [23%] had LVH detectable by Echocardiogram.

Of these 13 patients had LVH detectable by ECG.

Table No:11-LVH and Microalbuminuria

LVH	Total No: of cases	Microalbuminuria				
		Present		absent		
		No	%	No	%	
Absent	77	7	9.1	70	90.9	P < 0.001 χ^2 =54.48
Present	23	20	86.9	3	13. 1	

Figure No:11-LVH and Microalbuminuria



Among the patients with evidence of LVH by echo, a significantly higher proportion had microalbuminuria.(as p<0.05)

Abnormalities in LV Function-A total of 27 of 100 patients had Left ventricular dysfunction of which-

LV diastolic dysfunction-12

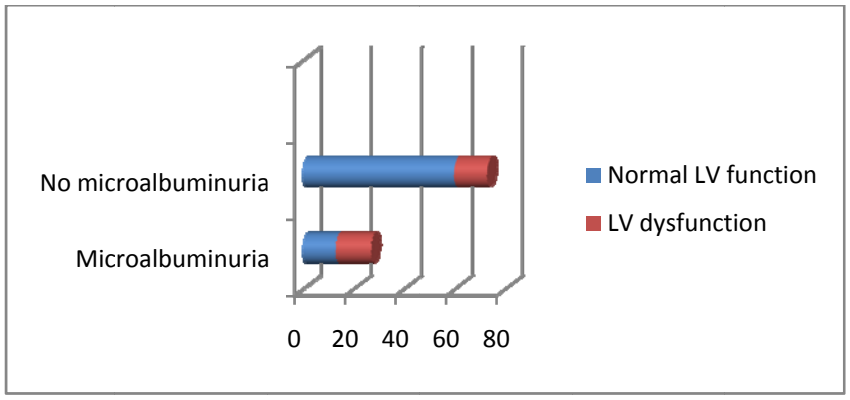
LV systolic dysfunction-9

Both LV systolic and diastolic dysfunction-6

Table No:12 – Abnormalities in LV Function & microalbuminuria

LV function	Total No: of cases	Microalbuminuria				
		Absent		Present		
		No	%	No	%	
Normal	73	60	82.2	13	17.8	P < 0.001 χ^2 =11.59
LV dysfunction	27	13	48.1	14	51.9	

Figure No:12 – Abnormalities in LV Function & microalbuminuria



Among the patients with LV dysfunction, the prevalence of microalbuminuria was higher and the difference was statistically significant. ($p<0.05$)Among study population, 19 patients had regional wall motion abnormalities (RWMA).

ABNORMAL ECHO FINDINGS IN STUDY GROUP:

Left ventricular hypertrophy:23

Left ventricular dysfunction:27

Regional wall motion abnormalities:19

Table No:13 –Coronary artery disease and Microalbuminuria

	Total No: of cases	Microalbuminuria				
		Present		absent		
		No	%	No	%	
No CAD	66	4	7.3	62	92.7	
Stable angina	4	3	75	1	25	p = <0.001 χ^2 =43.61
Unstable angina	14	10	71.4	4	28.6	
Myocardial infarction	16	10	62.5	6	37.5	

Presence of coronary artery disease has significant correlation to presence of microalbuminuria in systemic hypertension

Figure No:13 –Coronary artery disease and Microalbuminuria

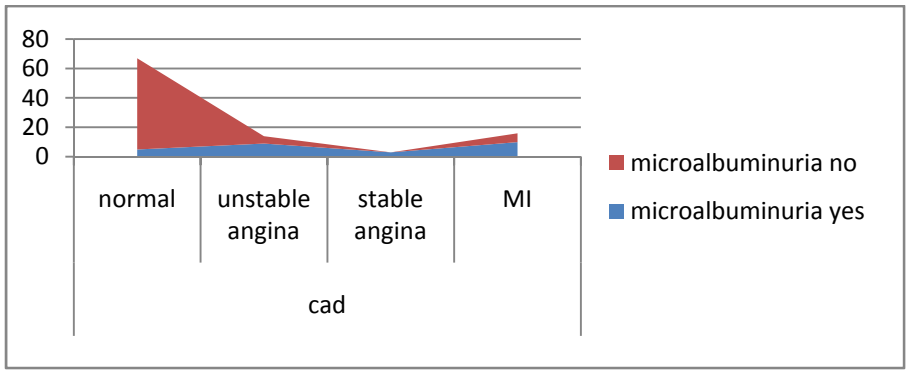


Table No:14- Relationship of microalbuminuria with various target organ damages.

Target organ damage	P value
Retinopathy	< 0.001
Left ventricular hypertrophy	< 0.001
Left Ventricular dysfunction	< 0.001
Coronary artery disease	<0.001
Cerebrovascular accident	0.61

Thus from above table ,we infer that *presence of microalbuminuria has statistically significant association with development of retinopathy,left ventricular hypertrophy ,coronary artery disease and left ventricular dysfunction while study showed no correlation between development of stroke and presence of microalbuminuria in systemic hypertension*

DISCUSSION

The present study evaluated the relationship of microalbuminuria with the indices of target organ damage in non diabetic hypertensives; correlation between microalbuminuria and age of the patient; duration and severity of hypertension and other cardiovascular risk factors.

Prevalence : The prevalence of microalbuminuria in this study was 27 %(27 out of 100 patients). In 1991 Stefano Bianchi et al published the first large study on the prevalence of microalbuminuria in hypertensives ; it was found to be – 35%. Palatini et al in HARVEST study and the PREVEND – IT (Prevention of Renal and Vascular End stage Disease – Study performed in the Dutch city of Groningen) showed a prevalence of 8 – 15%. Another study by Tsioufis et al in 2002 reported a prevalence of 47%.,while that Stamm et al reported it as 13.7% in 2006 [49] . The variability in prevalence may be explained by [12]:

1. Different values used to define microalbuminuria.
2. Different protocols used to evaluate microalbuminuria.
3. Difference in the methods of urine collection.
4. Characteristics of study population.

Sex distribution of microalbuminuria: In the present study, there was no significant difference between the prevalence of miroalbuminuria in men and women.[P= 0.08]. In the HUNT study (Norway) a stronger association was

observed between microalbuminuria and mortality in men than in women. In this study the interaction between sex and Albumin creatinine Ratio (ACR) was statistically significant (p= 0.003) and supported a sex difference, women had more prevalence. They attributed this difference to the higher incidence of asymptomatic UTI in women. They suggested the need for different ACR cut off values in men and women – because men have greater muscle mass and higher creatinine excretion than women although albumin excretion levels are equal[13]. (HUNT – Nord Trondelag Health Study). Pontremoli et al in the MAGIC study on the prevalence and clinical correlates of microalbuminuria observed that microalbuminuria was more common in males.

In the present study, microalbuminuria was found to have positive correlation with the duration [P<0.05] but not to severity of Hypertension.[p =0.83]. Pontremoli et al 1997 in the MAGIC Study have observed that degree and prevalence of microalbuminuria correlate with the height of BP when considering office values, even more so with 24 hour B P Cerasola et al and Ophsal et al had made similar observations[21].

Whether treatment of hypertension had any influence on microalbuminuria was studied.The difference in microalbuminuria in treated and untreated/irregularly treated hypertensives was not statistically significant.[p=0.94]. This observation may be due to the bias in classification of hypertensive patients to treated &

untreated groups based on the treatment history; though many patients are on drug therapy, adequate control was not achieved in many.

Microalbuminuria and other Cardiovascular risk factors: The present study also looked into the relation between microalbuminuria and other risk factors for cardiovascular disease like smoking, obesity and unfavourable lipid profile. Significant correlation was observed between smoking and microalbuminuria.[p=0.005]. This observation is concordant with that seen in previous studies on this aspect.

Microalbuminuria had no positive correlation with BMI in the present study[P=0.714]. This is not in agreement with most of the previous studies. Del O' mo et al (2003) had observed that microalbuminuria is more frequent in obese individuals. Leocini et al had observed greater BMI in patients with microalbuminuria ($p < 0.04$)[23,24]. Microalbuminuria was found to have no relation with unfavorable lipid profile(p=0.203). This is not in agreement with previous studies. Bianchi et al in 1997 had observed that hypertensive patients with microalbuminuria manifest increased serum LDL level and greater LDL/HDL ratio when compared with patients without microalbuminuria and normotensives[26].

RELATIONSHIP OF MICROALBUMINURIA WITH THE INDICES OF TARGET ORGAN DAMAGE:

Hypertensive Retinopathy

The present study showed a significant correlation between microalbuminuria and the presence and severity of retinopathy. ($p < 0.001$). Beisen et al in 1997 has observed an increased prevalence of hypertensive retinopathy in a group with persistent microalbuminuria despite adequate treatment. ($P < 0.03$)[21]. In 2002 Cerasola et al has observed a greater prevalence of Retinopathy among those patients with microalbuminuria[27].

Microalbuminuria and stroke

The present study included 26 patients with CNS involvement, 15 patients with CT showing infarct and 6 patients with CT showing hemorrhage,while 5 had normal CT study.Prevalence of microalbuminuria had no association to stroke ($P = 0.61$). It is contradictory to other studies which claim that microalbuminuria is a predictor of ischaemic stroke due to its well known association with carotid atherosclerosis (asymptomatic vascular events). There are many studies on the correlation between microalbuminuria and asymptomatic carotid artery disease – assessed by carotid intima – media thickness; Nuclear magnetic resonance imaging etc. In a study by Pontrermoli et al (2002), out of 279 patients studied, Urine albumin excretion was positively associated with carotid atherosclerosis. Patients

with increased UAE were 21 times more likely to develop increased carotid intima media thickness[8]. Leena et al (Stroke – 1997) Observed increased carotid IMT in patients with microalbuminuria ($P < 0.01$). In other studies, microalbuminuria has been shown to be a prognostic marker in ischemic stroke, even after accounting for confounding factors[29],while the current study failed to show any association.

Urine Albumin Excretion and Abnormalities in LV structure and function:

It was observed that 23 out of 100 (23%) patients had LVH detectable by ECHO. C. Tsioufis et al [2002] in their study observed that 21% of the 249 had LVH. LVH is reported in nearly 30% untreated hypertensives.

In the present study, it was observed that there is significant correlation between the prevalence of microalbuminuria and the presence of LVH ($P < 0.001$) and LV dysfunction ($P < 0.001$) in hypertensive patients. This aspect has been studied by many investigators. W.Kristian et al in 2002 (LIFE study) observed a higher prevalence of microalbuminuria 30% vs 9% in patients with concentric hypertrophy on ECHO ($P < 0.0001$)[15]. Pontremoli et al in 2002 has observed that patients with microalbuminuria were 21 times more likely to have both LVH ($P < 0.001$) in a study conducted in 279 patients in their institution[8]. C.Stefanadis et al made similar observation in 2002 – LVH was significantly higher in microalbuminuric patients compared with normoalbuminuric subjects (32 vs 5% $p < 0.0001$). The association between microalbuminuria and LV geometry may be

due to hemodynamic or non hemodynamic reasons. It is suggested that increased levels of ANP secreted from hypertrophic ventricles can directly cause microalbuminuria. The fact that subjects with heart failure and elevated ANP levels exhibit microalbuminuria gives further support to this view[29].

Microalbuminuria and coronary artery disease in systemic hypertension

The study included 34 hypertensive patients with coronary artery disease.Microalbuminuria showed a positive correlation to presence of coronary artery disease.($p<0.001$).This is in accordance to various international studies.The study by Jan Skov Jensen et al also clearly states that microalbuminuria in systemic hypertension is a predictor of coronary artery disease. Microalbuminuria is the strongest predictor of ischemic heart disease, with an unadjusted relative risk of 4.2 (95% CI 1.5 to 11.9, P=0.006) and a relative risk of 3.5 (95% CI 1.0 to 12.1, P=0.05) when adjusted for all other atherosclerotic risk factors, including age and gender. Study concludes that, microalbuminuria confers a 4-fold increased risk of ischemic heart disease among hypertensive or borderline hypertensive subjects.[30, 44]

The data from this study thus support the positive correlation between microalbuminuria and the duration of hypertension,smoking; the indices of target organ damage (except cerebrovascular accident) and various other cardiovascular risk factors.

CONCLUSIONS

- Hypertension is a major health problem in the community

- Microalbuminuria has a positive correlation with smoking,there by increasing risk of target organ damage in smoking population.

- Prevalence of microalbuminuria is more in those with longer duration of hypertension.

- Microalbuminuria is an integrated marker of cardiovascular risk and has statistically significant correlation with the presence and severity of target organ damage in systemic hypertension like retinopathy,left ventricular hypertrophy,left ventricular dysfunction and coronary artery disease.

- Microalbuminuria is a useful predictor of several target organ damages in systemic hypertension and hence should be utilized as a routine screening test in hypertensive population.

BIBLIOGRAPHY

1. Aram V. Chohanian, George L. Bakris; Henry R.Black, Daniel W.Jones, Suzanne Oparil. The Seventh Report of the Joint National Committee on Prevention, Detection Evaluation & treatment of High Blood Pressure; JAMA: May 21, 2003. Vol. 289.
2. Mancia G et al, 2007 Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology. Eur Heart J. 2007 Jun;28(12):1462-536
3. Jimmelman A, Recent hypertension guidelines : JNC-7 and ESH/ESC, Blood Press 2003 ,12 pp.196-197
4. Tagle R, Acevedo M, Vidt DG. Microalbuminuria: is it a valid predictor of cardiovascular risk? Cleve Clin J Med. 2003; 70 (3): 255-61.
5. Jensen JS, Feldt-Rasmussen B, Strandgaard S, Schroll M, Borch-Johnsen K. Arterial hypertension, microalbuminuria, and risk of ischemic heart disease. Hypertension. 2000; 35 (4): 898-903.
6. Redon J. Measurement of microalbuminuria — what the nephrologist should know. Nephrol Dial Transplant. 2006; 21 (3): 573-6.
7. H.L. Hillege; W.M. Jansen, D.E. Grobhee; G.F. Diecrks. – The PREVENT study group (2001). Journal of Internal Medicine Vol. 249; June 2001.

8. R.Pontremolli, G. Leoncini; M.Ravera; D.Parodi; C.Tomolillo Microalbuminuria; Cardiovascular and Renal Risk in Primary Hypertension – Journal of American Society of Nephrology 13: S (169-172); 2002.

9. Scott M. Grundy; J. Cleeman; L.Clark; R.Pasternak; S.Smith – Implications of Recent Clinical Trials for the NCEP – ATP III Guidelines. Circulation 2004: 110: 227-239.

10. Sukhija R, Aronow WS, Kakar P, Garza L, Sachdeva R, Sinha A, et al. Relation of microalbuminuria and coronary artery disease in patients with and without diabetes mellitus. Am J Cardiol. 2006; 98 (3): 279-81

11. Weir MR, Blantz RC. The clinical utilization of albuminuria as a surrogate measure of cardiovascular disease burden and risk for events: are we there yet? Curr Opin Nephrol Hypertens. 2005; 14 (1): 39-41.

12. C.Trioufis; C.Stefandis; M.Toutouza, Microalbuminuria is associated with unfavourable cardiac genetic adaptations in essential hypertensive subjects. Journal of Human Hypertension April 2002; Vol 16: P 249-254.

13. S. Romunstad; J. Holmen; H. Hallan, K. Kvenid; H.Ellekjaer. Microalbuminuria and all cause mortality in Treated Hypertensive individuals. The Nord Trondelag Health Study (HUNT Norway).

14. Bezante GP; Viazz F, Nicolella C; Berutti V; Brunelli C. Left ventricular Geometry & Function in patients with Essential hypertension & Microalbuminuria. Journal of Hypertension 17; 993-1000; 1999.

15. W.Kristian, P.Vittorio, Michael H; Jonathan N, Urine Albumin Creatinine Ratio and echo LV structure and function in Hypertensive patients with Microalbuminuria with echo evidence of LVH – The LIFE study. American Heart Journal. 143.2: 319-326. Feb. 2002.

16. Tuttle K.R; Ruhlmann ME; Cooney S.K. Urine albumin & Insulin as predictors of CAD – An angiographic study. American Journal of Kidney Disease; 34: 918 – 925 – 1999.

17. Berton G; Cordiano R; Mhaso S; DeToni R; Morimo R; Prognostic significance of Hypertension and albuminuria for early mortality after MI. Journal of HT: 16. 525-530; 1998.

18. Sacchi G; Deferrari G; Martionoli C; Delsette M: Microalbuminuria is can early marker of TOD in Essential HT. American Journal of Hypertension II: 430-438: 1998.

19. Pendrinelli R; Penno G; Bandinelli S; Giannini D; Dissociation between microalbuminuria and common carotid thickness in Essential HT men: Journal of Human HT 14: 831-835; 2002.

20. Nakamura S; Kawano Y; Inagana T; Horio T: Ikuda N: Microalbuminuria and CVS events in elderly hypertensive patients without previous cardiovascular complications – Hypertension 2003: 26: 603-608.

21. R.Pontremoli; A.Sofia; M.Ravera; C.Nicolella, N.Ruella. Previous Clinical correlates of microalbuminuria in Essential Hypertension MAGIC study: Hypertension 1977. 30: 1135-1143.

22. R.Bigazzi; S.Bianchi; Compese Von, Baldani G. Prevalence of microalbuminuria in large population with mild – moderate Essential HT: Neprhon 1992. 61: 94-97.

23. Dell Omo, Giuseppets; Di Bello; Vitantonsa G; R.Pendrinelli Journal of Hypertension 21 (6); 1163-1169. June 2003.

24. Michael H; Bjorn Sheley; Rosetta M; Pederson J. Microalbuminuria & Essential HT. Current opinion in Nephrology & Hypertension 8 (3): 359-363. May 1999.

25. G.Leoncini; F Viazzi; V.Vaccao, A.Parodi. AJH 2006; Nov. 19 (11): 1183-89.

26. D.Baldani G; R. Bigazzi; Nenci R; S.Bianchi. Microalbuminuria in Essential HT: Journal of Nephrology. Vol. No.4: 1997. P 216-218.

27. Cerasola G; Cottore S; D'Ignoto; Grasso L. Microalbuminuria points out early renal and CVS damages in EH: Revista Latina De Cardiologia; 2002: 13: 3.

28. G.Pellegrini; R. Pendrinelli; G. Dell Omo' V.Di Bello – Low grade inflammation and microalbuminuria in HT. Atherosclerosis Thrombosis & Vascular Biology – 2004; 24: 2414.

29. C.Tsioufis, K.Dimitriadis; D.Antioniadis, C.Stefanadis. Inter relationship of microalbuminuria with other surrogates of Atherosclerotic vascular disease in Hypertensive subjects. American Journal of Hypertension; 2004; 17: 470-476.

30. Jan Skov Jensen; Bo Feldt-Rasmussen; Svend Strandgaard; Marianne Schroll; Knut Borch-Johnsen. Arterial Hypertension, Microalbuminuria, and Risk of Ischemic Heart Disease. *Hypertension.*2000;35:898.)

31. Giovanni Cerasola1, Giuseppe Mulè, Santina Cottone,Emilio Nardi, Paola Cusimano.Hypertension, microalbuminuria and renal dysfunction: the Renal Dysfunction in Hypertension (REDHY) study. Jnephrol 2008; 21: 368-373.

32. Sarnak MJ, Levey AS, Schoolwerth AC, et al. Kidney disease
as a risk factor for development of cardiovascular disease:
a statement from the American Heart Association

Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Hypertension. 2003;42:1050-1065.

33. The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC).2007 guidelines for the management of arterial hypertension. J Hypertens.2007;25:1105-1187.

34. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure. The JNC 7 Report. JAMA. 2003; 289 (19): 2560-71.

35. Yuyun MF, Khaw KT, Luben R, Welch A, Bingham S, Day NE, et al. Microalbuminuria, cardiovascular risk factors and cardiovascular morbidity in a British population: the EPIC-Norfolk population-based study. Eur J Cardiovasc Prev Rehabil. 2004; 11 (3): 207-13.

36. Ljungman S, Wikstrand J, Hartford M, Berglund G. Urinary albumin excretion — a predictor of risk of cardiovascular disease: a prospective 10-year follow-up of middle-aged nondiabetic normal and hypertensive men. Am J Hypertens. 1996; 9 (8): 770-8.

37. Campese VM, Bianchi S, Bigazzi R. Is microalbuminuria a predictor of cardiovascular and renal disease in patients with essential hypertension? Curr Opin Nephrol Hypertens. 2000; 9 (2): 143-7.

38. Tagle R, Acevedo M, Vidt DG. Microalbuminuria: is it a valid predictor of cardiovascular risk? Cleve Clin J Med. 2003; 70 (3): 255-61.

39. Kopyt NP. Slowing progression along the renal disease continuum. J Am Osteopath Assoc. 2005; 105 (4): 207-15.

40. Klausen K, Borch-Johnsen K, Feldt-Rasmussen B, Jensen G, Clausen P, Scharling H, et al. Very low levels of microalbuminuria are associated with increased risk of coronary heart disease and death independently of renal function, hypertension, and diabetes. Circulation. 2004; 110 (1): 32-5.

41. Jacobs Jr DR, Murtaugh MA, Steffes M, Yu X, Roseman J, Goetz FC. Gender- and race-specific determination of albumin excretion rate using albumin-to-creatinine ratio in single, untimed urine specimens: the Coronary Artery Risk Development in Young Adults Study. Am J Epidemiol. 2002; 155 (12): 1114-9.

42. Agrawal B, Berger A, Wolf K, Luft FC. Microalbuminuria screening by reagent strip predicts cardiovascular risk in hypertension. J Hypertens. 1996; 14 (2): 223-8.

43. Ratto E, Leoncini G, Viazzi F, Vaccaro V, Parodi A, Falqui V, et al. Microalbuminuria and cardiovascular risk assessment in primary hypertension: should threshold levels be revised? Am J Hypertens. 2006; 19 (7): 728-34; discussion 735-6.

44. Ana Maria Nunes de Faria Stamm; Gisele Meinerz; Jacqueline Consuelo da Silva. Systemic hypertension and microalbuminuria. Arq. Bras. Cardiol. vol.89 no.6 São Paulo Dec. 2007.

45. Wang TJ,Evans JC,Meigs JB,D'Agastino et al,Low grade albuminuria and the risks of hypertension and blood pressure progression.Circulation 2005;111:1370-6

46. Keane WF, Eknoyan G. Proteinuria, albuminuria, risk, assessment, detection, elimination (PARADE): a position paper of the National Kidney Foundation. Am J Kidney Dis. 1999; 33 (5): 1004-10.

47. Mogensen CE, Vestbo E, Poulsen PL, Christiansen C, Damsgaard EM, Eiskjaer H, et al. Microalbuminuria and potential confounders: a review and some observations on variability of urinary albumin excretion. Diabetes Care. 1995; 18 (4): 572-81.

48. Ruilope LM. Kidney dysfunction: a sensitive predictor of cardiovascular risk. Am J Hypertens. 2001; 14 (6 Pt 2): 213S-217S.

49. Stamm AM, Meinerz G, Silva JC. Systemic hypertension and microalbuminuria. Arquivos brasileiros de cardiologia. 2007 Dec;89(6):415-20

50. Cleland SJ, Sattar N, Petrie JR, Forouhi NG, Elliott HL, Connell JM. Endothelial dysfunction as a possible link between C-reactive protein levels and cardiovascular disease. *Clin Sci (Lond).* 2000; 98: 531–535

51. Clausen P, Jensen JS, Jensen G, Borch-Johnsen K, Feldt-Rasmussen B. Elevated urinary albumin excretion is associated with impaired arterial dilatory capacity in clinically healthy subjects. *Circulation.* 2001; 103: 1869–1874

PROFORMA

MICROALBUMINURIA IN SYSTEMIC HYPERTENSION

AND ITS RELATIONSHIP TO TARGET ORGAN DAMAGE

PROFORMA FOR DATA COLLECTION

CASE NO: NAME :

NO: AGE: SEX:

DURATION O HYPERTENSION :

SYMPTOMS:

PAST HISTORY: DIABETES MELLITUS/CHRONIC RENAL FAILURE/OTHER CO-MORBID ILLNESSES

PAST ADMISSIONS:

SMOKING:

DURATION: TYPE: FREQUENCY:

ALCOHOL INTAKE:

DURATION: AMOUNT: TYPE :

FREQURENCY:

MENSTRUAL STATUS

HEIGHT : WEIGHT: BMI :

PERIPHERAL PULSES:

BP- SITTING: STANDING :

SYSTEMIC EXAMINATION-

CVS SKIN:

RS: EYE:

ABD: BONE:

CNS: FOOT:

PNS: DENTAL:

LABORATORY EXAMINATION

URINE

ALB: SUGAR: ACETONE: PUS CELLS:

URINE CULTURE & SENSITIVITY:

URINE ALBUMIN/CREATININE RATIO:

BLOOD

HB: TC: DC: ESR: PLATELETS:

UREA: CR: FBG: PPBG:

CHOL: TG: HDL: LDL:

ECG

CHEST X-RAY

OPTIC FUNDUS

ECHOCARDIOGRAPHY

CT BRAIN

DETAILS OF DRUG THERAPY

MASTER CHART

NO.	Name	Age	SEX	Duration	Treatment	SBP	DBP	smoking	BMI	RBS	B Urea	S.Cr e	TC	TGL	HDL	ACR	MA	CT	Fundus	LVH	LV fn	CAD
				(years)		(mm of Hg)				(mg/dl)			(mg/dl)			(micro gram/mg)		(mm)				
1	Velingiri	68	M	4m	Reg	136	80	yes	27.8	112	26	0.6	158	156	66	20.8	no	_	hazy	no	Normal	UA
2	Rajan	66	M	11	Reg	164	100	yes	20	88	32	0.8	126	150	47	11.3	no	_	Normal	no	Diastolic	MI
3	Sarasammal	60	F	3	Reg	144	80	no	19.2	116	36	0.8	138	155	32	6.88	no	_	hazy	no	Normal	MI
4	Rabiya	58	F	2	Reg	128	76	no	19.4	98	32	0.8	172	144	62	25.6	no	_	Normal	no	Normal	MI
5	Pelarisamy	48	M	2	Irrg	150	90	no	28.3	84	23	1.2	168	126	56	23.5	no	_	hazy	no	S&D	MI
6	Rajammal	44	F	new	No	146	80	no	26.1	116	30	0.6	220	164	30	12.3	no	_	1	no	Normal	N
7	Nataraj	57	M	4	Irrg	124	82	yes	20.8	112	28	0.8	155	118	58	150	yes	H	Normal	no	Diastolic	UA
8	Rasiya	53	F	2	No	114	70	no	23.5	130	24	1.1	195	276	50	50.1	yes	N	Normal	no	Normal	SA
9	Nagammal	60	F	1	Irrg	150	90	no	40.2	126	36	0.6	153	92	42	28.7	no	_	Normal	no	Normal	N
10	Rajathi	58	F	1	Reg	156	98	no	18.8	111	22	1	175	101	45	13.4	no	_	Normal	no	Normal	N
11	Ayyavu	52	M	3m	Irrg	110	70	yes	22.2	114	32	0.8	162	134	46	4.16	no	_	3	no	Normal	N
12	Rajkumar	54	M	5m	No	144	80	yes	23.9	92	27	1.2	168	122	43	27.4	no	H	3	no	Normal	N
13	Rafik	65	M	13	Irrg	150	90	yes	19.9	114	29	1	154	155	34	12.7	no	__	Normal	no	Normal	MI
14	Ramkumar	62	M	new	No	154	96	yes	32.1	122	30	1	184	132	59	22.1	no	_	hazy	no	S&D	MI
15	Velraj	50	M	2	Reg	146	86	yes	20.6	86	36	0.8	165	116	45	26.4	no	_	Normal	no	Normal	N
16	Mathankumar	48	M	2	Irrg	120	80	yes	35.2	94	32	0.6	148	160	45	27.7	no	_	Normal	no	Diastolic	N
17	Nalini	40	F	3	Irrg	146	80	no	25.3	116	24	1.2	178	148	53	16.4	no	N	hazy	no	Normal	N
18	Fathima	42	F	2	Reg	152	90	no	30.9	80	36	0.8	250	229	21	8.69	no	N	Normal	no	Normal	N
19	Rajeshwari	56	F	2m	Reg	132	70	no	18.8	130	32	1	169	134	60	21.3	no	_	1	no	Normal	N
20	Subbal	54	F	6m	Irrg	122	78	no	21.3	134	26	1.1	160	178	52	25.9	no	_	2	no	Normal	N
21	Kumar	69	M	6	Reg	148	80	yes	31.1	122	28	1	142	133	28	56.6	yes	N	4	no	Diastolic	UA
22	Selvaraj	66	M	8	Irrg	146	90	no	32	116	28	1.2	146	162	48	10.9	no	N	Normal	no	Normal	N
23	Sivakumar	54	M	3	Irrg	148	96	yes	36.5	86	30	1	134	104	58	27	no	I	Normal	no	Diastolic	N
24	Gauder	53	M	1	Reg	126	70	yes	32.5	82	26	0.8	190	188	46	18	no	_	Normal	no	Normal	N
25	Nagaraj	52	M	7m	Reg	122	78	no	26.1	114	34	1.2	143	122	58	9.87	no	_	hazy	no	Normal	N
26	Selvakumar	58	M	1m	No	150	90	no	19.9	116	36	1.2	136	150	52	12.3	no	H	2	no	Normal	N
27	Abubaker	62	M	new	No	136	84	yes	21.1	126	35	0.6	138	130	46	25.6	no	_	2	no	S&D	N

NO.	Name	Age	SEX	Duration	Treatment	SBP	DBP	smoking	BMI	RBS	B. Urea	S.Cr	TC	TGL	H DL	ACR	MA	CT	Fundus	LVH	LV fn	CAD
				(years)		(mm of Hg)					(mg/dl)			(mg/dl)		(microgram/mg)		(mm)				
28	Sujatha	60	F	1	Reg	152	80	no	20.8	120	28	0.6	240	260	36	13.8	no	_	2	no	Normal	N
29	Ambika	55	F	1	Irrg	148	90	no	19.3	98	31	1.1	186	188	58	18.6	no	_	2	no	Normal	N
30	Kalaivani	42	F	3	Irrg	160	110	no	19.6	86	28	0.8	160	155	60	24.5	no	_	2	no	Normal	N
31	Prabha	54	F	4	No	150	88	no	23.9	78	29	1	132	136	54	11.3	no	_	2	no	S&D	N
32	Jogarammal	75	F	4	Reg	148	90	no	21.6	112	35	0.6	184	108	70	23.9	no	_	2	no	S&D	N
33	Saranya	76	F	1	Reg	158	96	no	22	114	25	1.2	188	112	62	11.2	no	_	2	no	Normal	N
34	Veeran	46	M	4m	Reg	138	94	no	19.8	136	34	1	166	134	53	10.1	no	I	2	no	Normal	N
35	Janaki	50	F	6m	No	130	70	no	22.3	126	24	0.8	140	166	30	19.7	no	_	2	no	Normal	N
36	Pakusamy	56	M	8m	Reg	128	80	no	21.5	122	38	1	220	180	60	23.5	no	_	2	no	Normal	N
37	Jaya	59	F	2	Irrg	142	90	no	19.3	128	34	1	218	238	36	14.5	no	I	2	no	S&D	N
38	Kuppan	60	M	4	Irrg	144	94	yes	18.9	82	31	0.6	132	140	52	194	yes	_	4	yes	Diastolic	UA
39	Ramasamy	58	M	9	Reg	136	94	yes	23	78	27	1	188	190	64	143	yes	_	hazy	yes	Normal	MI
40	Selvaraj	67	M	8	Reg	164	100	yes	23.5	118	30	0.8	160	150	58	43.3	yes	_	2	yes	Normal	MI
41	Mani	65	M	6	No	148	92	yes	22.8	112	23	1	230	198	38	87.7	yes	I	hazy	yes	S&D	N
42	Swaminathan	60	M	4m	No	146	98	yes	27.8	132	35	1.2	120	104	46	134	yes	_	1	yes	Diastolic	UA
43	Kuppathal	56	F	2	Reg	158	94	no	21.9	94	33	1.2	202	160	32	211	yes	H	4	no	Normal	SA
44	Baby	68	F	4	Reg	144	90	no	27.7	80	22	1.1	212	184	40	160	yes	_	2	no	Normal	UA
45	Muthusamy	50	M	4	Irrg	138	96	no	21.5	76	32	0.8	140	100	52	10.9	no	_	4	yes	S&D	SA
46	Ponnusamy	53	M	3	Reg	170	118	no	19.2	126	36	1.1	180	190	58	8.9	no	_	2	yes	Normal	N
47	Jayaraman	59	M	2	Reg	130	92	yes	18.8	78	32	0.6	152	164	62	36.7	yes	_	1	yes	Diastolic	MI
48	Prabhakaran	62	M	1	Reg	146	80	yes	19.9	112	29	1.1	240	200	38	111	yes	I	1	yes	Normal	UA
49	Sumathi	59	F	8	Irrg	166	120	no	23	126	33	0.8	194	184	30	65.7	yes	_	2	yes	Normal	N
50	Kabeer	70	M	7	Reg	150	94	no	28.6	76	36	1.2	137	110	46	181	yes	_	2	yes	Systolic	UA
51	Muthammal	60	F	3m	Irrg	146	86	no	23.1	102	24	0.6	110	90	40	132	yes	_	4	no	Normal	N
52	Prema	62	F	7m	Irrg	130	70	no	22.6	88	25	1	180	240	30	12.6	no	_	2	no	Normal	N
53	Balamani	45	F	2	Irrg	140	94	no	24.1	94	32	1.2	247	110	43	40.9	yes	I	2	yes	Normal	SA
54	Selvi	47	F	4	Reg	150	88	no	21.9	88	35	1	146	90	55	64.2	yes	I	2	yes	Systolic	MI
55	Latha	56	F	6	Reg	152	86	no	26.9	114	33	1.1	135	120	53	10.8	no	_	1	no	Normal	N
56	Vasanthi	58	F	3	Reg	138	90	no	21.8	128	24	0.6	183	117	58	28.8	no	_	2	no	Normal	N
57	Ponnammal	60	F	2m	Irrg	136	80	no	24.7	122	37	1.2	180	110	56	5.66	no	_	2	no	Normal	N
58	Meena	65	F	8m	No	130	76	no	32.6	92	31	1	182	210	59	14.6	no	_	2	no	Normal	N
59	Lakshmi	56	F	5m	Irrg	146	90	no	21.8	86	30	1.1	173	192	62	21.7	no	_	3	no	Systolic	N

NO.	Name	Age	sex	Duration	Treatment	SBP	DBP	smoking	BMI	RBS	B.Urea	SCr	TC	TGL	HDL	ACR	MA	CT	Fundus	LVH	LV fn	CAD
				(years)		(mm of Hg)				(mg/dl)			(mg/dl)			(microalbuminuria)	(mm)				
60	Leela	52	F	new	Reg	122	80	no	19.8	84	33	1.2	190	160	56	12.9	no	-	2	no	Normal	UA
61	Amudhan	56	M	7m	Reg	150	90	no	18.6	120	24	1.1	180	140	64	24.8	no	I	3	no	S&D	N
62	Ganeshan	58	M	4m	No	110	70	yes	24.2	112	35	0.6	130	110	48	23.3	no	-	hazy	no	S&D	N
63	Velu	43	M	<1	Irrg	118	80	yes	27.3	132	33	1.2	118	80	42	13.2	no	-	3	no	Systolic	N
64	Sajudheen	47	M	new	No	166	104	yes	24.2	88	32	0.8	162	170	58	25.5	no	-	2	no	Normal	N
65	Karthika	62	F	1m	Reg	138	74	no	23.5	78	26	1	230	200	34	80.6	yes	-	3	no	Systolic	UA
66	Perumal	67	M	7	Irrg	170	110	no	27.4	68	38	1.2	128	100	38	51.2	yes	-	3	no	Normal	N
67	Rangathal	48	F	1	Reg	150	90	no	26.9	126	26	1	180	140	48	11.3	no	-	2	no	Normal	N
68	Samiappan	47	M	2	Reg	128	84	yes	21.7	122	34	1.2	138	104	54	21.4	no	-	3	no	S&D	UA
69	Sajna	42	F	9m	Irrg	130	78	no	26.6	120	28	0.6	145	80	52	22.4	no	-	2	no	S&D	N
70	Kamalam	44	F	10m	Irrg	130	70	no	21.2	98	28	0.8	136	130	57	11.2	no	-	2	no	Normal	N
71	Ramathal	61	F	3	Reg	146	92	no	24.3	128	31	1.1	162	148	58	23.7	no	-	2	no	Normal	UA
72	Saraswathi	65	F	3	Irrg	146	90	no	24.1	130	35	1	200	108	40	28.6	no	-	hazy	no	Normal	N
73	Meenakshi	46	F	new	No	174	116	no	21.2	120	32	1.2	160	128	36	15.4	no	-	2	no	Systolic	N
74	Sujatha	48	F	3m	Irrg	142	90	no	20.8	94	25	1.1	238	110	42	17	no	-	Normal	no	Normal	UA
75	Raji	70	F	15	Reg	128	80	no	22.1	88	38	1.1	120	100	32	147	yes	I	Normal	yes	Diastolic	UA
76	Abdulwahab	78	M	3	No	136	80	tes	24.8	128	35	1	180	138	54	77.4	yes	-	2	yes	Diastolic	MI
77	Ponnulakshmi	45	F	5m	Reg	128	76	no	19.6	124	33	1.2	186	150	38	9.56	no	-	Normal	no	Normal	N
78	Jayakumari	59	F	3m	Irrg	142	94	no	23.7	84	32	1	246	220	32	26.7	no	-	Normal	no	Normal	N
79	Rani	50	F	6m	Reg	180	120	no	27.8	80	27	1.1	220	250	31	15.7	no	-	hazy	no	Normal	N
80	Jagadambal	69	F	3m	Irrg	210	130	no	24.1	74	34	0.8	190	230	38	21.5	no	-	3	no	Normal	N
81	Yasoda	68	F	9	Reg	150	88	no	23.8	116	30	1.1	166	190	55	8.98	no	-	3	yes	Normal	MI
82	Thenmozhi	46	F	2	Irrg	220	150	no	23.4	92	28	0.8	175	186	57	37.9	yes	-	Normal	yes	Normal	N
83	Malarvalli	48	F	9	Irrg	156	80	no	24.7	94	32	1.2	248	179	34	21.6	no	-	hazy	no	Normal	N
84	Geetha	57	F	6	Reg	138	94	no	27.4	88	30	1	116	130	52	22.2	no	-	2	no	Normal	N
85	Kannan	68	M	8	Irrg	130	80	yes	24.1	128	26	1	145	180	45	17.5	yes	I	Normal	yes	Diastolic	MI
86	Kathirvel	66	M	9	Irrg	116	78	yes	28.3	126	24	0.6	138	160	52	25.7	yes	I	3	yes	Normal	MI
87	Anitha	40	F	6m	Reg	120	70	no	22.2	122	26	1.1	206	190	35	13.3	no	-	Normal	no	Normal	N
88	Loganath	48	M	5m	Irrg	144	90	yes	23.7	116	26	1	152	180	52	25.7	no	-	Normal	no	Normal	N
89	Prabhu	46	M	3	Reg	110	78	yes	28.3	134	24	1.2	139	185	63	12.6	no	H	Normal	no	Normal	N
90	Ayyasamy	78	M	2	Reg	180	112	yes	21.1	136	26	0.8	168	156	64	18.5	no	I	hazy	no	Normal	N
91	Saravanan	68	M	5m	Irrg	148	94	yes	20.3	98	28	1	176	184	55	86.1	yes	I	3	yes	S&D	MI

NO.	Name	Age	SEX	Duration	Treatment	SBP	DBP	smoking	BMI	RBS	Blood Urea	S.Cr e	TC	TGL	HDL	ACR	MA	CT	Fundus	LVH	LV fn	CAD
				(years)		(mm of Hg)				(mg/dl)			(mg/dl)			(mcg/mg creatinine)		(new)				
92	Arumugam	62	M	7	Irrg	114	84	no	20.9	88	32	1	170	225	42	36.7	yes	_	Normal	yes	Diastolic	N
93	Rema	75	F	3	Irrg	128	80	no	24.3	80	30	1	220	210	36	19.4	no	_	Normal	no	Normal	N
94	Marafral	57	F	2	Reg	156	94	no	24.9	120	26	1.1	240	180	56	10.5	no	_	1	no	Systolic	N
95	Hamsa	68	M	9	Reg	142	90	yes	23.6	124	31	1	235	190	64	23.7	no	I	2	yes	Normal	N
96	Radhakrishnan	78	M	2m	Irrg	166	96	no	23.7	90	34	1.2	155	205	28	20.9	no	I	Normal	no	Systolic	N
97	Krishnaveni	59	F	8m	No	118	70	no	29.5	86	24	0.6	190	186	38	8.43	no	_	hazy	no	Normal	N
98	Shanmugam	78	M	4	Irrg	146	78	yes	23.4	80	32	1	234	210	42	9.87	no	_	Normal	no	Systolic	N
99	Rajan	64	M	6	Irrg	116	80	yes	24.3	118	30	0.8	185	220	38	164	yes	I	1	yes	S&D	MI
100	Maran	72	M	2	Reg	120	70	no	27.5	106	28	1	265	220	38	10	no	_	Normal	no	Normal	N

ABBREVIATIONS IN MASTER CHART

Duration of hypertension:m=Months,new=newly detected hypertension.

Optic fundus: 1= grade 1 hypertensive retinopathy,2=grade 2 hypertensive retinopathy,3=grade 3 hypertensive retinopathy,4=grade 4 hypertensive retinopathy

CT Brain :N=Normal,H=Hemorrhage,I=Infarct

Coronary artery disease: UA=unstable angina, SA=stable angina,MI=Myocardial infarction

LeftVentricularDysfunction:DIASTOLIC=diastolic dysfunction,SYSTOLIC=systolic dysfunction,S &D=both systolic and diastolic dysfunction.

Treatment history-No-not on treatment,Irrg=Irregular treatment,Reg=Regular treatment

INFORMED CONSENT FORM

Project title:

"MICROALBUMINURIA IN SYSTEMIC HYPERTENSION AND ITS RELATIONSHIP TO TARGET ORGAN DAMAGE "

This is a project to detect the prevalence of microalbuminuria in systemic hypertension and its relationship to target organ damage Your participation will help us to identify the presence of microalbuminuria in hypertension and will help in appropriate interventions.All information collected from you for this purpose will be kept confidential and names will not be disclosed.

I _____ fully understand the project and have no objection in the researchers using any of my information for the purpose of research. My signature below indicates that I voluntarily agree to participate in this study. I will receive a copy of this consent form.

Name of the worker:

Name of the witness:

Signature of the worker:

Signature of the witness:

Date :

ABBREVIATIONS

ACEI: Angiotensin Converting Enzyme Inhibitors

ACR: Albumin Creatinine Ratio

ARB: Angiotensin Receptor Blocker

BMI:Body Mass Index

BP : Blood Pressure

BUN: Blood Urea Nitrogen

CAD: Coronary Artery Disease

CCF: Congestive Cardiac Failure

CT: Computerised Tomography

CVA:Cerebro Vascular Accident

DBP: Diastolic Blood Pressure

ECG: Electrocardiogram

HDL*: High-Density Lipoprotein*

HT: Hypertension

JNC: Joint National committee

LDL: Low-Density Lipoprotein

LV: Left Ventricle

LVH: Left Ventricular Hypertrophy

MI: Myocardial Infarction

MRI: Magnetic Resonance Imaging

RAAS: Renin-Angiotensin-Aldosterone System

SBP: Systolic Blood Pressure

TG: Triglycerides

UAE: Urine Albumin Excretion